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The Journal of Allergy

VOL. II MAY, 1931 No. 4

Original Articles

THE HEREDITARY FACTOR IN HYPERSENSITIVENESS. ANAPHYLAXIS AND ALLERGY*

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LONDON, ENGLAND

A DISEASE is understood to be hereditary when it is transmitted as an integral part of the male or female germinal cells to the product of union of these two cells, occurring through the medium of their chromatin and cytoplasmic structures, and transmitted from generation to generation in fairly definite numerical ratios.

At once it is evident that all diseases characterized by the phenomena of hypersensitiveness do not fall into this category. In animals, with but a possible exception, these manifestations can only be induced and such sensitization only transmitted to one generation. In man, a large percentage of cases of allergy show a positive familial taint, but in other cases no such trait can be determined, and we are compelled to admit that such a condition must have been acquired.

Nevertheless, the family history is positive so generally as to warrant a term to designate such predisposition when present, and that of *diathesis* is suggested which, though incapable of precise explanation, has the advantage of custom being employed in medical literature since before Hippocrates' day. Its capability for proper application to this phenomenon will be inferred from the definition given by Jonathan Hutchinson in his lectures on "The Pedigree of Disease" in 1884 as implying any bodily condition however induced in virtue of which the individual is, for a long period or usually through the whole life, prone to suffer from some particular form of disease. Some diatheses are inherited, others acquired; of some the effects are permanent or constant, in others they are transitory or recurrent after intervals of health.

Many terms have been suggested to designate this factor, such as, "Exudative diathesis" (Czerny), "Allergic disposition" (Van Leeu-

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wen), "Eosinophilic diathesis" (Strauble), "Allergic constitution" (Kammerar).

I. MODES OF INHERITANCE

Hypersensitiveness, in its clinical applications, would appear to be possible of transmission from parent to offspring in one of two modes.

A. Germinal or Chromosomal.—This is a true Mendelian inheritance taking place through the germ plasm of the mother or the father or both, and is the only possible method of transmission from an affected father. It is permanent in duration and capable of being passed on to succeeding generations in definite numerical ratios. It is always associated with a contrasted character, one being dominated over the other. In this condition one might consider the two genes hypersensitive the dominant and nonhypersensitive the recessive.

B. Placental or Serum Sensitization.—In the biologic sense this is not a true hereditary transmission as it is in no way connected with the germ plasm of the parents being due to direct placental permeability. Ratner and Kuttner have shown that the animal kingdom may be divided into several groups according to certain histologic differences in the placentas. In human beings and guinea pigs only a single layer of cells separates the fetal from the maternal circulation, and in these the placenta is extremely permeable to the passage of many forms of heterologous substances.

According to the nature of the substance transmitted through this cellular layer the type of fetal sensitization may be divided into:

1. Active, where the sensitizing agent affecting the mother acts directly on the cells of the fetus, and
2. Passive, where the antibodies produced by the mother in response to the sensitizing agent are transmitted to the fetus.

II. MANNER OF INHERITANCE

A. Anaphylaxis in Animals.—Up to the present it has not been shown definitely that a true germinal hereditary influence plays any part in the anaphylactic reactions of animals, or that sensitivity can be transmitted from an affected male parent. One preliminary observation, for which I am much indebted to Mr. A. D. Buchanan Smith of the Animal Breeding Research Department of the University of Edinburgh, may be of this nature. It refers to the seasonal occurrence of "hay fever" over several years in a herd of pedigree Jersey cattle kept under excellent conditions.

In the summers of 1923 and 1924 it was noticed that a few cows suffered from slight nasal discharge, and in 1925 a few heifers were affected as well. Autumn 1926 a few more cows were affected. In the summer of 1927 six cows out of eight and four heifers out of seven were affected. The nasal discharges showed remarkably few organisms and spraying their cultures on the nasal mucous membrane of a cross-bred

crow failed to reproduce symptoms. In all cases the trouble quickly disappeared when the animals were housed and symptoms reappeared immediately on allowing one of the most affected cows out to grass for a few hours on a warm dry day. Cross-bred cattle were not affected though in the same field, nor the bulls due to the custom of keeping them in all the summer. Symptoms occur from the beginning of June to the beginning of October, though in 1928 the disease appeared about the middle of May and in offshoots of the herd as well. The affected animals run predominantly in one line, but considerable inbreeding is present in the herd.

Placental transmission or serum sensitization is the common form induced in animals. It cannot be transmitted from a sensitive male parent or to a third generation.

1. Active sensitization may occur by the passage through the placenta of heterologous serum injected into the pregnant female. Positive results are not very common, for the amount of heterologous serum passing through the placenta and penetrating the organism of the fetus is too weak, in general, for sensitization. When it does occur, it is done to unchanged antigen. If the injection of serum is made some short time before the birth of the litter, the young are not sensitive the moment of birth and do not become so till some days have elapsed. This sensitivity then lasts for some three to four months.

2. Passive sensitization is due to the passage through the placenta of maternal antibodies. The progeny may be subjected to anaphylactic shock from the day of their birth but lose their sensitivity in less than three months. This type is the more easily induced and the more frequent in occurrence.

B. Allergy in Man.—In considering any hereditary factor the obtaining of perfect agreement with Mendelian ratios in the allergic diseases to which human beings are subject is a matter of extreme difficulty. In the first place, it is difficult to tell whether the manifestation was brought about by definite germinal transmission or as a result of sensitization while in utero. Second, it is impossible to control the material; matings occur as one finds them, not as one wishes. Third, generations are long and families not large enough to feature all possible combinations of factors. Fourth, records are inadequate and fragmentary and subject to vast inaccuracies. Fifth, even in individuals with an abnormal capacity for sensitization artificial sensitization is not an easy accomplishment. Others possessing the tendency may not manifest it at all, or have manifested it in a form not recognized or remembered. In addition the factor may exist in young children and not show as a clinical state later in life. Finally, the extreme multiplicity of types and causes, the same cause giving rise to many types, and the same type arising from different causes; the numerous routes of entrance of these excitants into the body; and the fact that

sensitization may depend on some factor other than the mere administration of native heterologous protein all add greatly to the confusion.

1. Historical.—Most writers have realized the important rôle played by the hereditary factor in asthma. Sennertus (1650) described how his wife's father, two brothers, a sister and a sister's daughter all labored under the complaint. Sir John Floyer (1698) stated, "As my asthma was not hereditary from my ancestors, so, I thank God, neither of my two sons are inclined to it, who are now past the age in which it seized me." Cullen (1784) and Ryan (1793) both suggested its hereditary transmission. Davidson (1795) gives an account of an illustrative case. Hereditary transmission appeared the generally accepted opinion in America according to the writings of Eberle (1831) and Goode (1836). Ramadge (1835) gave an account of the disease in four successive generations. Andral (1839) mentioned heredity as one of the prime factors predisposing to asthma. Salter (1860) in a study of thirty-five cases determined a positive family history in thirteen. Later, in 1868, he found distinct traces of inheritance in eighty-four of 217 cases, the kind differing very much; sometimes it was direct, sometimes lateral; sometimes immediate, sometimes remote. Steavenson (1879) described how he had inherited his asthma from his paternal grandmother. Geddings (1883) stated, "That this tendency is hereditary in nature is conceded by every prominent writer on asthma." Drinkwater (1909) recorded a very impressive pedigree.

The influence of heredity in hay fever was first suggested by Phoebus (1862). Wyman (1872) noted that fifteen out of seventy-seven cases showed more than one member in the same family affected. Beard (1876) found sixty-six of 190 cases, while Mackenzie (1884) found it positive in 40 per cent of his patients.

The familial occurrence of migraine has been a subject of comment since the beginning of the eighteenth century. Tissot (1834) drew attention to it, and it is interesting to observe how the percentage incidence noted has mounted since that day: Symonds (1858) found 44 per cent, Liveing (1873) 50 per cent, Henchen (1881) 64 per cent, Moebius (1894) 90 per cent, Auerbach (1913) and Smith (1922) 100 per cent.

Dinkelacher (1882), in the same year as angioneurotic edema was first identified by Quincke, noted its occurrence in a watchmaker and his son. Valentin (1885) observed another son in the same family affected. Strubling (1885) observed a father, son and daughter affected and Osler (1888) twenty-two members in five generations.

2. Modes.—(a) Germinal or Chromosomal. Obviously this is the only manner in which any hereditary predisposition may come from the father. From the study of the family histories of several hundred cases of allergy in children I found that the inheritance may have been bilateral in 17 per cent and unilateral in 51.5 per cent. In these

unilateral cases the family history was on the mother's side twice as often as on the father's. Most observers agree that the allergic proclivity is inherited, and most discussion ranges round the mode of inheritance, whether as a dominant or recessive Mendelian factor. If it were a true Mendelian factor in the biologic sense the percentage figures of descendants affected should be: (1) if dominant Mendelian. and if affected ancestry are bilateral—100 per cent, if unilateral 50 per cent, and no affected ancestry 0 per cent; (2) if recessive Mendelian character, comparable figures would be 100 per cent, 50 per cent, 25 per cent. Spain and Cooke, from a study of 1,889 cases found that when the inheritance was double 69.4 per cent of the offspring were affected, when single 58 per cent, and when entirely negative 41.1 per cent. Obviously the conditions of chromosomal inheritance are not fulfilled in these cases.

Possibly this apparent discrepancy may be explained by supposing one manner of inheritance is truly chromosomal in which males, females or both may be transmitters. Some cases in which no family history is evident may have been actively sensitized in utero, in which case it is not necessary for the mother to manifest symptoms.

(b) Placental or Serum Sensitization. Active sensitization is brought about by the direct influence of the sensitizating agent transmitted through the placenta of the mother to the cells of the fetus. Ratner, from a careful investigation of the antepartum history of the mother in some fifteen cases of food allergy in infants, adduced substantial evidence that a mother's overindulgence in certain protein foods during gestation may lead to an active sensitization in utero of the child. After birth, on coming in contact with this food for the first time, the child may manifest some form of allergic phenomenon even though the mother did not manifest any sensitivity either before or during gestation.

Passive sensitization may be produced by the passive transfer of antibodies from a sensitized mother, in which case it is necessary for both mother and child to show the same sensitization, but this is not the rule according to clinical observations. Cooke and Vander Veer compared the sensitization of the antecedents and descendants in a large series of cases and concluded that this type of sensitization cannot be an important method because: (a) In cases where the inheritance has been maternal, the clinical form in the child is much more likely to be different from that of the mother than it is to be identical (as 5 is to 2), and is no more likely to be identical with that of the mother than with that of the father. In children whose aunts and uncles are sensitive the clinical type is just as likely to be identical with that of the uncle or aunt as it is to be like that of the parent. (b) In six pairs of twins, three pairs had identical sensitization, but in none was the mother

herself affected. In two pairs inheritance was maternal alone, and the sensitization was identical with that of the mother once and different once.

An apparently normal person whose antecedents and whose brothers and sisters are sensitized frequently does transmit something to the offspring, but of what this factor consists it is difficult to say.

The differences between anaphylaxis in animals and allergy in man as far as any hereditary factor is concerned are apparent. Germinal transmission has not been reported in animals but is frequent in man. Active sensitization in utero is difficult in animals, but possible in man. Passive sensitization is the common mode in animals, but rare in all probability in man. The modes in the two species appear diametrically opposite.

OBSERVATIONS

I have studied the family history in 200 consecutive cases of asthma in children up to twelve years of age. In all 4,152 relatives were considered, an average of more than twenty per patient. The manifestations particularly inquired for were asthma, hay fever, eczema, urticaria and migraine. Due care was taken to exclude such "positive" cases as asthma commencing late in life or in the presence of known renal or cardiac disease; sneezing of an occasional nonseasonal and nonenvironmental nature; eczema of but short duration or of a presumably occupational etiology; urticaria only occurring occasionally as a child

TABLE I

	MALES		FEMALES		TOTAL	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
TOTAL CASES	145	72.5	55	27.5	200	
FAMILY HISTORY						
Unilateral	78	75.7	25	24.3	103	51.5
(a) Mother's side	48	73.0	18	27.0	66	64.0
(b) Father's side	30	81.0	7	19.0	37	36.0
Bilateral	22	64.7	12	35.3	34	17.0
Nil	45	71.4	18	28.6	63	31.5
TOTAL RELATED PERSONS						
Affected	342	57.3	255	42.7	597	14.3
Unaffected	1712	50.9	1650	49.1	3362	81.0
Transmitters	64	33.2	129	66.8	193	4.7
Grand total	2118	51.0	2034	49.0	4152	
INDIVIDUAL DISEASES						
Asthma	278	63.5	160	36.5	438	73.3
Hay fever	17	46.0	20	54.0	37	6.2
Eczema	92	63.4	53	36.6	145	24.3
Urticaria	51	68.9	23	31.1	74	12.4
Migraine	13	27.0	35	73.0	48	8.0

INHERITANCE									Total
Father	A	A	A	T	T	U	U	T	
Mother	A	T	U	U	A	A	T	T	
Families	7	4	14	21	8	21	45	17	137
Affected	43	32	56	54	43	87	133	79	527
Transmitters	6	12	5	30	13	8	70	49	193
Unaffected	51	38	75	170	68	118	314	149	983

A = Affected, T = ? Transmitter, U = Unaffected.

TABLE II

RELATIONSHIP BETWEEN AGE, SEX, AND FAMILY HISTORY

AGE AT ONSET	UNILATERAL			BILATERAL			NIL			GRAND TOTAL		
	M.	F.	TOTAL	M.	F.	TOTAL	M.	F.	TOTAL	M.	F.	TOTAL
0- 1	20	3	23	4	3	7	11	3	14	35	9	44
1- 2	12	5	17	8	2	10	5	5	10	25	12	37
2- 3	10	6	16	3	2	5	6	1	7	19	9	28
3- 4	11	3	14	2	2	4	7	1	8	20	6	26
4- 5	10	2	12	3	1	4	4	4	8	17	7	24
5- 6	5	4	9	2	1	3	5	–	5	12	5	17
6- 7	6	1	7	–	–	–	3	1	4	9	2	11
7- 8	3	1	4	–	1	1	1	–	1	4	2	6
8- 9	–	–	–	–	–	–	1	2	3	1	2	3
9-10	1	–	1	–	–	–	1	–	1	2	–	2
10-11	–	–	–	–	–	–	1	1	2	1	1	2
Totals	78	25	103	22	12	34	45	18	63	145	55	200

and at extremely isolated instances in later life; or migraine that did not give more than one of the characteristic ocular, cerebral or abdominal symptoms. The results are summarized in Table I.

The main points that these figures would seem to indicate are: (a) Age Incidence. Most observers have shown in dealing with cases at all ages that the greater or more complete the inheritance, the earlier the age at which symptoms will have their onset. This is true even during the first decade. Although one out of five cases develops symptoms during the first year irrespective of hereditary influences, in cases with bilateral inheritance practically all have had their onset before the sixth year, with unilateral inheritance before the eight year, while those with negative history still continue up to puberty.

(b) Sex Incidence.—In this series there were 145 males and 55 females. Among the 4,152 related persons considered the sexes were fairly evenly distributed—males 51 per cent, females 49 per cent. The total affected persons in the group were males 342, females 255. If we subtract the children patients from these figures we find that the sex incidence among the remaining affected relatives is practically identical —males 197, females 200. This slight preponderance of affected females from puberty onward is characteristic of the figures of most observers:

Walker	400 cases	198 males	202 females
Bullen	265 "	131 "	134 "
Coke	172 "	71 "	101 "

It would appear that, if from birth to puberty the sex incidence of males to females is greater than 2 : 1, and from puberty onward less than 1 : 1, then puberty must be a definite decisive milestone toward which a great number of males must improve, and beyond which a greater number of females develop symptoms, or at which there is a change in the type of allergic manifestation. It is suggested that puberty must exert some beneficial effect upon the symptoms in the

male and some deleterious effect upon the female. This fact is in full accord with the life histories one often hears in these asthmatics. How often does the father say that he suffered from asthma till he left school or began to work, or the mother assign the onset of her trouble to post-school years or marriage! When we consider the transmitters—sons or daughters of allergic parents who, while not showing any symptoms of allergy in themselves, have a child or children who manifest the allergic state—we note again that the proportion of females to males is as 2 : 1. Also in cases with a unilateral history we notice that transmission is twice as often through the mother's side as through the father's, and in tabulating the inheritance particulars twice as many are affected with allergy where the male is unaffected and the female has or may transmit the tendency as when the male is affected or a transmitter and the female quite free.

In summary, such figures suggest that the inheritance of allergic manifestations is twice as frequent through the female as through the male, and twice as many offspring are likely to be affected when the female transmits. Of the offspring over twice as many males as females are likely to be affected before puberty; the probability of recovery at puberty is much greater in the boy than in the girl; and the chance of developing allergic manifestations after that age is more probable in the female than in the male. A positive family history was determined in 68.5 per cent of the cases, in 51.5 per cent unilateral, in 17 per cent bilateral.

3. Individual Manifestations.—Before passing on to the discussion of the individual manifestations, a few figures are necessary as to the general incidence of allergic manifestations among normal families. Balyeat found 8.3 per cent of some 1,117 students were of families in which some allergic disease was present. Spain and Cooke found a history of asthma or hay fever in 3.5 per cent of 119 normal families, and Cooke and Vander Veer in 7 per cent of 204. Therefore one is fairly safe in assigning its maximum incidence as 10 per cent in the families of normal persons. In allergic families the frequency of manifestations is distinctly higher. Smith shows a tree of 87 persons in 5 generations, 37 of whom are allergic.

ASTHMA

In asthmatic children the following observations as to the percentage incidence of a positive family history of allergy have appeared. Bullen in 235 cases: 50.7 per cent. Comby in 75 cases 58 per cent were hereditary with similar manifestations, 46 per cent hereditary with dissimilar manifestations. Peshkin in 278 cases: 42.5 per cent. Rowe in 110 cases under twenty years: 70.9 per cent, 19.1 per cent bilateral, 51.8 per cent unilateral. Schloss in 80 cases: 47 per cent.

In asthmatic adults, Adkinson in 400 cases found 48 per cent, Bullen

in 500 cases: 39.4 per cent, Coke in 350 cases: 46 per cent, Menagh in 300 cases: 40 per cent, Rackemann in 150 cases: 58.7 per cent in sensitive cases, 10.7 per cent in non-sensitive, Rowe in 234 cases: 58.4 per cent, in 45 cases: 65.2 per cent, Salter 217 cases: 39 per cent, Van Leeuwen in 49 cases: 63.6 per cent.

Drinkwater's pedigree would seem to indicate the inheritance of asthma as a simple dominant character, but such pure asthma lineages are extremely rare, other evidences of the allergic diathesis generally appearing. Fantham has described what must be a unique experience, 17 cases of asthma due to rabbit hair sensitiveness in 5 generations comprising 25 individuals. The tendency appears as a simple dominant, but one apparently normal woman transmits it to both children.

HAY FEVER

Scheppegrell, in 1,000 cases of hay fever found that 358 had relatives of the first degree (parents, brothers or sisters) affected with hay fever. Kahn in 100 cases found 80 per cent. Spain and Cooke in 462 cases: 58.4 per cent, in 51.1 per cent unilateral and in 7.3 per cent bilateral. Cooke and Vander Veer in 504 cases found 48.4 per cent.

FOOD ALLERGY

The susceptibility of many members of the same family to various foods is a well-known fact, and the family described by Laroche is frequently quoted. Outside Rowe's figures of a positive family history of allergy in 68 per cent of 175 cases of food allergy, there are very few statistics dealing with this aspect.

DERMATOSES

Piness and Miller found a positive family history in 41 per cent of cases. Regarding eczema, O'Keefe and Rackemann in 239 children found 28 per cent, but in 37 per cent of adult cases. Rackemann alone found 36 per cent of cases in children and 50 per cent of adults. Rowe in 16 cases found 69 per cent, Balyeat in 76.6 per cent, in 12.3 per cent bilateral, in 64.3 per cent unilateral. Regarding urticaria, Menagh in 260 cases found 32.6 per cent, Rowe in 20 cases 55 per cent, and Rackemann and Colmes 25 per cent.

ANGIONEUROTIC EDEMA

Since Osler in 1888 described 22 cases of this affection in 5 generations comprising 36 members, a great number of similar observations have been made. But in these cases where the condition is handed on from generation to generation in definite Mendelian proportions, where there is a great tendency for death to occur from edema of the glottis, I doubt if a true allergic diathesis is at the root. Though foods are often incriminated, there does not appear any definite case reported

where skin tests or elimination diets have revealed such a causative factor in this distinctly familial type. Such families have been reported by Crowder and Crowder, Mendel, Fritz, Ensor, Campbell, Bullock and McDowall (quoted by Whiting).

But sporadic instances of angioneurotic edema do occur among the members of allergic families. These do give positive protein reactions, and the symptoms abate when the cause is removed. Phillips has described a similar condition in dogs hypersensitive to protein. Attacks have also occurred as one of the reactions induced through attempts at desensitization.

ICHTHYOSIS

This is a rare condition which is generally hereditary. But typical ichthyosis occurs in about 5 per cent of asthmatic children, and other members of their family are frequently affected. This proportion is a good deal higher than among the general population and is sufficient to suggest that its presence in several members was more than an accidental occurrence.

MIGRAINE

In this condition again the same two definite types are apparent. In the distinct familial type transmission is an expression of a Mendelian phenomenon. Mills has traced migraine through 5 generations, and Tileston has found that 50 per cent show direct heredity even for three or four generations. Rowe in 30 cases, Diamond in 35, Bramwell in 61, and Liveing in 53 found a large percentage show direct transmission, mostly through the mother. Buchanan found that in 100 families where one parent suffered from migraine 22.6 per cent of the children were affected, in 3 families where inheritance was bilateral all children were affected, and in 17 families where neither of the parents was affected 26 per cent of the children suffered. Allan, in a study of 500 cases, found in 56 families where both parents had migraine 83.3 per cent of the children were affected, in 240 families where one parent was affected 62 per cent of the children were affected, and in 98 families where neither parent had migraine only 3.7 per cent of the children suffered.

Sporadic cases occur in the families of allergic individuals, especially in the mothers of asthmatic children. Vaughan recounts 10 cases of migraine in a series of 33 in which specific sensitiveness to various foods could be shown and which were cured by mere avoidance of these foods. Balyeat considers this hereditary factor a most potent one. An allergic family history was found in 85.4 per cent of 55 cases, and in 45.4 per cent migraine itself. In 67.3 per cent of the cases other manifestations of allergy were present. Ball, in 1,000 unselected family histories found 261 cases of migraine associated with migraine in 45.9 per cent, 162 cases of asthma associated with migraine in 37 per cent, 91 cases of

hay fever associated with asthma in 49.4 per cent and with migraine in 38.4 per cent, and eczema associated with eczema in 21.3 per cent and migraine in 40.9 per cent. Rowe found a positive family history of allergy in 74 per cent of 86 cases of migraine due to food allergy.

DRUG ALLERGY

The influence of heredity in drug allergy has not been investigated. Lewin has recorded instances of allergy to the same drug in parent and child as well as in sisters.

SERUM SICKNESS

Here again the hereditary factor has not been investigated. Von Pirquet and Schick mention an instance of sisters being the subjects of serum disease.

EPILEPSY

Spangler studied 100 cases and found 77 instances of migraine among the ancestors (F:M::2:1), 44 instances of asthma (F:M::2:1) 17 of urticaria (F:M::3:1), 12 of hay fever (F:M::2:1), and 8 of eczema (F:M::1:1). I do not find epilepsy at all common in the family histories of allergic children, nor have I even been able to obtain positive skin reactions in some score of cases tested.

From the foregoing observations and statistics it is obvious that asthma, hay fever, eczema, urticaria, and some cases of angioneurotic edema, ichthyosis, and migraine are diseases intimately related both in the individual and his family. From their comparative infrequency in the families of normal individuals it is fair to assume that some definite tendency or diathesis must be transmitted.

III. NATURE OF INHERITANCE

As to the true nature of this inheritance very little is known or has been suggested. Statistical surveys have merely shown that the majority of allergics have one or more antecedents with some recognized form of allergy, and that a certain proportion of the children of allergic parents will develop symptoms. Others of these children, while not manifesting any sensitivity themselves may again transmit the tendency to their children. What appears to be transmitted is a tendency to develop a sensitiveness of some kind to some substance: though the offspring of hay fever sufferers are more likely to suffer from hay fever than asthma and the reverse, it is general for numerous other manifestations to appear in the same individual and in many members of his family. This hereditary transmission cannot be that of hypersensitiveness to a particular protein or group of proteins, since the causative allergen generally differs in parent and offspring. What does appear to be transmitted is an unusual capacity for developing specific reactivities to various foreign proteins, and the point which concerns us is the

nature of this factor in the offspring which determines such ability to manifest symptoms of allergy.

A. Particular Disease or Tissue? Cases do occur where a particular type of allergy is transmitted from generation to generation, and pure asthma or hay fever lineages have been well illustrated in the literature, as well as the unique instance of Fantham's where the same allergen was responsible for all cases. It is possible that in many of these cases other allergic manifestations were not inquired for or had been forgotten by the patient. With regard to angioneurotic edema, ichthyosis and migraine it is extremely doubtful whether the pure familial types are true allergic responses, and no definite positive evidence has yet been adduced to prove this contention. On the other hand sporadic cases frequently do occur in the members of allergic families, give positive skin reactions, and do not reappear after the offending allergen has been removed. On account of the extreme vagaries in the type of response in different individuals in the same families, it is obvious that it cannot be a specific disease that is transmitted from parent to offspring.

Coca inclines to the view that a particular tissue or shock organ is inherited, and while admitting the close interrelationship of the various allergies, concludes that definite shock tissues are subject to separate inheritance, thereby postulating a general and an individual transmission. A definite shock tissue, the unstriped muscle, does occur in lower animals, and the varied sites of reaction in the different species depend upon anatomic peculiarities in the distribution of this muscle, which appears to be the only shock tissue involved. From this fact it is assumed that the same principle holds in all forms of specific sensitiveness. But a shock tissue in the human has not been definitely identified to embrace such numerous sites of reaction as the skin, the mucous membranes of the eye, nose, lungs and alimentary tract, as well as the subcutaneous tissues.

Still we are at a loss to explain how in two persons, both sensitive to the same substance as shown by the Prausnitz-Kustner reaction, one suffers only from hay fever and the other only from asthma. Or again, on testing the skin of a case of allergic eczema with the specific exciting agent a wheal results, not a patch of eczema, indicating that some other factor is concerned in addition to the tissue, excitant and the specific reagins. All we do know is that in a normal person these sites are not susceptible to specific influences as they are in the allergic, and every allergic individual does not show an equal susceptibility of all these sites.

B. Particular Susceptibility to Effects of Reaction? For many years investigators have ascribed all allergic symptoms to a hypersensitive neurocellular mechanism, and French authors for some thirty years have postulated a specific bulbar center which is hyperexcitable to the

effects of these allergic reactions. Hurst inclines to the view that there is an overactivity or predominance of the bronchomotor portion of the vagus.

A special nervous temperament has frequently been described as characteristic of these allergic individuals and endeavors have been made to ascribe the transmission of the diathesis to this nervous or psychic pattern. One often notes in discussing an allergic child with parents that they tend to show exaggerated mental responses. Such tendencies to a disturbance of mental balance certainly run in families, and Cammidge has collected histories which suggest that their inheritance follows Mendelian laws. Frequent endeavors have been made to track down these altered reactions and ascribe them to various portions of the nervous system. Others explain these nervous states on the theory of adrenal exhaustion. Two theories are worthy of further comment.

Vasomotor Instability.—Kolmer finds that vascular reactions are the outstanding and prominent tissue changes in human allergy, due largely to the involuntary musculature. He suggests that persons with sensitive vasomotor systems should be more susceptible to the effects of allergy than the more stolid individuals, and that it is possibly through this channel that both irritants and emotions may act. For it is generally known that humans are more susceptible to reaction than lower animals, whites than negroes, adults than children, and highly strung individuals than the more stolid and lowly.

Vago-Sympathetic Imbalance.—Eppinger and Hess classify neurotics into (a) sympathicotonics, with overactive sympathetic displayed by tachycardia, overaction of thyroids, adrenal, and pituitary, a tendency to high blood pressure a raised blood sugar, excessive thermal reactions to infections, and temperamentally liable to phobias; (b) vagotonics, with overactive vagus displayed by slow pulse, liability to syncope, spastic constipation, low blood sugar, and allergic reactions. They react badly to infections and temperamentally are of vague apprehension. In these allergic conditions this hypothetical overaction of the vagus may be relative rather than absolute, an underacting sympathetic may tip the balance in favor of the vagus.

That this balance does bear some relationship to the reciprocal action of the endocrine glands is well known, and one is at a loss to decide whether it is the nerves that influence the glands or the glands which influence the nerves.

Slight alterations in the biochemical make-up of the individual can produce such vast alterations in his reactions, and it is possible that such a biochemical factor may underlie these peculiar nervous reactions.

C. Endocrine dysfunction? The organs of internal secretion play an undeniable rôle in the symptomatology of allergic reactions. This is plain from the rapid amelioration of symptoms that takes place on the injection of adrenalin in practically all sufferers, as well as the frequent

beneficial effect of parathyroid, thyroid and pituitary extracts. Such therapeutic benefits led Drummond to postulate a suprarenal deficiency as directly or indirectly responsible for the symptoms. Other observers have noted that hyperthyroidism increases and hypothyroidism decreases the inclination toward allergic reactions and that parathyroid hormone tends to prevent symptoms. Hurst considers that proteins have a depressing effect on the action of the endocrine glands and hence on the sympathetic system. Others ascribe the nocturnal periodicity to the fact that the endocrines are at rest during sleep. This remains without visible influence on normal human beings because there is a sufficient reserve of glandular secretion produced during the day to tide over the system during sleep. With suprarenal dysfunction the adrenal reserve is deficient, and during sleep the sympathetic receives no external impressions as there is no adrenalin reserve to disturb it in its rest. The vagus being on duty both day and night remains active and alert and so reacts to any impression or irritant. The female sex glands appear to have a pronounced effect. Many females show a tendency for attacks of asthma just before or during menstruation which respond to ovarian therapy. In others they cease during pregnancy and the puerperium, while pollen sensitivity does not appear to be affected at all. On the other hand I have seen mothers who get attacks only during gestation.

D. Particular Biochemical Make-up? It is in this sphere that the most likely solution to the problem lies. Slight alterations in the body's physicochemical equilibrium can lead to profound changes in its reaction to disease. The fact that at altitudes of over 4,000 feet asthmatic paroxysms disappear, each individual having a particular altitude of freedom, forms a potent argument in supporting this view. To my mind such effect is due to changes in the acid-base equilibrium of the blood, but many other theories have been advanced and will be discussed first.

Calcium Deficiency.—Calcium is supposed to have an antiedemic action, checking the tendency to exudative processes by decreasing the permeability of the cell membranes. Sir Almroth Wright (1896) recommended its use in allergy on empirical grounds from its effect in urticaria, and Paramore (1905) and Osler (1907) surmised that an abnormal calcium metabolism underlay the urticarial tendency. Recent biochemical researches in allergy confirm that the physiologically available calcium is present in the blood in adequate amounts, and that calcium therapy in allergic conditions does not appear to produce permanent increase in the blood calcium. This may be due to the effect that the absorption of calcium depends on the hydrochloric acid of the gastric juice converting the calcium into a soluble salt and the absorption of this salt from the acid medium of the upper part of the small intestine. In allergies this may not be possible on account of the marked hypo-

chlorhydria so frequently present. Again, other observers have suggested that it is the potassium-calcium ratio or the blood calcium-phosphorus product that is altered.

Uric Acid or Gouty Diathesis.—French authors in particular have assigned to this diathesis a dominant rôle in the allergic predisposition, but when one considers their figures such an assumption is not justified. Bouchard only found 9 cases of asthma in 100 of gout, Lecorche 5 in 150, while See describes 14 cases of gout in 370 asthmatics. In 600 family histories I only have 2 in which any relative suffers from gout, both grandfathers, and in each case there is a history of allergy in the family of the other parent. In addition allergic diseases appear to be on the increase while gout is certainly on the decline.

Colloidoclasic Disequilibrium.—Widal has interested himself in this class of reaction in anaphylactic animals and describes similar reactions in allergic individuals. But this type of reaction takes place whenever large quantities of any protein are suddenly thrown into the blood stream and is not solely an integral part of the allergic response.

Acid-Base Disequilibrium.—This is the view that I favor, and contrary to most previous observers, I consider that allergics have a tendency to store up much alkali reserve without becoming definitely alkalotic. In studying the biochemistry of the blood of allergic children it would appear that during the free intervals the plasma bicarbonate is always above or at the higher limits of the normal range for children, and above that of their nonaffected brothers and sisters. As a result of the attack the level falls to the lower limit or to the acid side, and during this time the child is not susceptible to further attacks. If it can be kept at this level there is freedom from attacks. Again, in these children it would appear that the hypochlorhydria is a conservative effect, the nonsecretion or retention of the acid radicles tending to maintain the acid-base equilibrium. Many observations have been reported that tend to substantiate this view.

Spangler found that there is a slightly larger range of H-ion concentration in the blood of allergic than in nonallergic persons. Hemingway found that there is an increasing reaction of mammalian blood vessels to successive slight changes in the H-ion concentration toward the alkaline side, and concluded that these slight changes had a marked sensitizing action. Choremis found that acid therapy greatly lessened the allergic symptoms of tuberculin sensitiveness in a series of children. Tiefensee, in studying bronchial asthma, found that there was an alkalotic disturbance of the acid-base equilibrium. Lowering of the alkali reserve by means of a hunger day or an acid-producing diet rendered it possible to cut short or prevent symptoms. Schneider, from an intensive study of the biochemical changes induced by altitude, found that at a barometric pressure of 656 millimeters of mercury

corresponding to an altitude of 4,000 feet the alveolar carbon dioxide pressure and the per minute volume of breathing were found to be changed. He showed that the total alkalinity or alkaline reserve of the blood is reduced in inhabitants at high altitudes and that good toleration at these heights is dependent upon an ability to eliminate quickly excess of blood alkalies.

Many other points as mentioned by Beckman are worthy of note: (a) peptic ulcers are rare in allergics; (b) diabetics, though frequently acidotic or ketotic, are rarely allergic; (c) starvation produces acidosis and a decline in allergic manifestations; (d) pregnancy also lowers the alkali reserve and decreases the manifestations; (e) acute infectious diseases and sea voyages are frequently accompanied by a clinical acidosis and an absence of allergic symptoms; (f) calcium therapy is in effect acid therapy, for when calcium chloride is given by mouth the calcium ion is combined with base and passed out in the feces, while the Cl ion is absorbed and hence the relative proportion of fixed acid in the body is increased. Sohlmann says that the blood calcium cannot rise materially above the normal limits unless the acid-base equilibrium is shifted toward the acid side. Hence the absence of a rise noted in calcium therapy in allergic individuals, and if a rise is obtained it is only by increasing the relative acidity of the medium.

In summary, most recent observations point to the particular make-up of the allergic individual from the biochemical standpoint as one of potential alkalosis.

IV. RESULTS OF INHERITANCE

A. On Age at Onset of Symptoms.—The nature of the inheritance plays a potent part in predetermining the age at which offspring of allergic parents will begin to manifest symptoms. This is apparent even during the first decade, for, as has already been shown in my cases, practically all those with bilateral inheritance had had their onset before the sixth year, those with unilateral inheritance before the eighth, while those with negative history still continue up to puberty.

Balyeat in a study of 1,000 cases of allergy in general found that when the inheritance was bilateral 58.6 per cent manifested symptoms in the first decade, 10 per cent in the second, and only 0.3 per cent after thirty years. When the inheritance was unilateral only 32.3 per cent appeared in the first decade and 30.8 per cent during the second. Spain and Cooke in a study of 462 cases of asthma and hay fever found that in 34 cases with bilateral family history, in 52.9 per cent symptoms began during the first five years of life and 26.4 per cent in the second five years, making a total of 79.1 per cent during the first decade, and all had begun to show symptoms before thirty-five years of age; in 236 cases with unilateral family history 36.3 per cent had commenced in the first decade and 29.6 per cent during the second; and in 192 cases

without a positive family history 21.7 per cent commenced during the first decade, 16.1 per cent during the second, and 39.4 per cent in the third. Cooke and Vander Veer, in studying 504 cases of hay fever found that symptoms began before the fifth year in 36.3 per cent of individuals with bilateral inheritance, in 14.3 per cent with unilateral, and in only 5.1 per cent of those without demonstrable inheritance. Symptoms began before the tenth year in 66.2 per cent of those with bilateral inheritance, in 32 per cent with unilateral, and in 17.7 per cent with none. After forty years none with bilateral inheritance develop symptoms, only 2.8 per cent with unilateral, and 7.1 per cent of those without history. In migraine, Balyeat has shown that 29 per cent develop symptoms in the first decade, 27 per cent in the second, 25 per cent in the third, and 18 per cent over thirty years.

In cases of asthma family histories are more frequently obtained in children than in adults. Rowe found them present in 70.9 per cent of 110 cases of asthma in children and in only 58.4 per cent of 234 asthmatics at all ages. Bullen found positive family histories in 50.7 per cent of 235 cases in childhood and in only 28 per cent of 265 cases in adult life.

Peshkin, in a series of 278 asthmatic children compares the age at onset with the family history, and my 200 cases are also set out for comparison.

Age at onset	1	2	3	4	5	6	7	8	9	10	11	12	13	
Peshkin's History														
Positive	35	21	17	10	10	7	4	5	6	1	0	0	1	117
Negative	40	32	19	15	12	10	10	7	8	4	1	1	2	161
My History														
Bilateral	7	10	5	4	4	3	–	1	–	–	–			34
Unilateral	23	17	16	14	12	9	7	4	–	1	–			103
Nil	14	10	7	8	8	5	4	1	3	1	2			63

From a consideration of the figures one is justified in confirming the finding that the more complete the inheritance the earlier the age at onset of manifestations.

B. On Skin Reactions.—Positivity. The findings of most observers agree with those of Adkinson, who, in a study of 400 cases of asthma, concluded that those of the sensitive type more frequently give positive family histories than do those of the nonsensitive type.

Multisensitivity. In allergic manifestations, reactions to multiple substances are the rule rather than the exception, but cases with positive family histories tend to give well above the average number of positive skin reactions.

C. On Manifestations.—Number. This point has been admirably stressed in a paper by Rackemann and Colmes, from which the following table is abstracted. As the number of manifestations in the same patient increases we note the relative increase in the percentage of positive as compared with negative family histories.

FAMILY HISTORY	NUMBER OF DIFFERENT MANIFESTATIONS IN THE SAME PATIENT			TOTAL NUMBER OF PATIENTS
	ONE	TWO	THREE OR MORE	
Positive	383 (35%)	154 (46%)	34 (63%)	571 (39%)
Negative	706 (65%)	183 (54%)	20 (37%)	909 (61%)

Type. Though various allergic manifestations appear in different members of allergic families, there is a definite tendency for the offspring of hay fever sufferers to suffer from hay fever rather than asthma and vice versa.

D. Number of Progeny Affected.—Spain and Cooke have shown that according to the variations in the inheritance of allergic conditions from the parents definite proportions of the progeny may be expected to develop symptoms at different ages. In 32 cases with bilateral inheritance, the total number of children was 83, of which 50 were allergic by the time they had reached seventeen years, from which they estimated that 71.6 per cent of children with a bilateral family history will eventually develop an allergic condition. In 211 families with unilateral inheritance 321 of 666 children were allergic before the age of 34 years, and therefore 56.1 per cent of children with unilateral family history will eventually develop symptoms.

CONCLUSIONS

1. One is not justified in endeavoring to explain the transmission of the allergic diathesis solely according to Mendelian laws as two modes appear to be involved:

(a) germinal, or true Mendelian, through the germ plasm of the parents.

(b) placental or serum sensitization, not truly hereditary being an active or passive fetal sensitization in utero.

Statistical surveys have shown merely that the majority of allergics have one or more antecedents with some type of allergic manifestation, and that a certain proportion of children of allergic parents will develop manifestations. Other of these children, while not manifesting any sensitivity themselves, may again transmit the tendency to their children.

2. In comparing the influence of the hereditary factor in anaphylaxis of animals with that of allergy in man, the two appear diametrically opposite; germinal transmission has not been reported in animals but is frequent in man: active sensitization in utero is difficult in animals but possible in man: passive sensitization is the common mode in animals but rare in man.

3. From my own observations it would appear that:

(a) The greater or more complete the inheritance, the earlier the age at which symptoms will have their onset is confirmed even during the first decade; for, when the inheritance is bilateral, practically all

cases have had their onset before the sixth year, when unilateral before the eighth year, while those with negative history still continue up to puberty.

(b) The diathesis is transmitted twice as often through the mother as through the father, and twice as many offspring are likely to be affected when the female transmits. Of the offspring over twice as many males as females are likely to be affected before puberty; the probability of recovery at puberty is much greater in the boy than in the girl; and the chance of developing allergic manifestations after that age is more probable in the female than in the male.

(c) A positive family history was determined in 68.5 per cent of cases, in 51.5 per cent unilateral, in 17 per cent bilateral.

4. There is no positive proof that the distinctly familial types of angioneurotic edema, migraine, or ichthyosis, or in our experience epilepsy, are of an allergic nature.

5. The nature of the allergic diathesis would appear to be that of a particular biochemical make-up, a tendency to store up much alkali reserve without becoming definitely alkalotic.

6. The greater or more complete the hereditary influences:

(a) the earlier the age at which symptoms will have their onset,
(b) the more frequent are skin reactions as to positivity and multisensitivity,
(c) the greater the number of manifestations,
(d) the greater the number of progeny affected, and
(e) the more likely are the progeny to show the same allergic manifestation as the parents.

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ELIMINATION DIETS FOR THE DIAGNOSIS AND TREATMENT OF FOOD ALLERGY*

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THE importance of food sensitivity in many allergic diseases has long been recognized, but it was not until 1928 that a systematic method of determining the causative foods by test diets was reported by Rowe.[1] His method was to place the patient for periods of a week or two on a series of diets each rigidly limited to a small number of foods and to observe the effects of these diets on the patient's symptoms. An effort was made to exclude foods to which many patients were sensitive and yet to maintain a diet which was adequate for a limited time. If symptoms were not relieved by use of the first diet, a second test diet was tried. If symptoms were relieved, new foods were added gradually in the succeeding weeks, excluding any that caused a recurrence of symptoms. Wheat, eggs, and milk were not added for several weeks. The building up of a satisfactory diet may take a long time with possible danger resulting from a restricted diet. In order to overcome the slight deficiency of minerals, especially calcium, in Rowe's diet, Dale and Thornburg[2] devised two diets composed of twenty-one and twenty-three mutually exclusive proteins, the unusual being used in preference to the common foods. Care was taken to include the foods which were rich in mineral and vitamin content. Though these diets were adequate, the diagnostic advantage of Rowe's limited diets was lost to some extent as the individual effect of each food could not be so carefully observed. More recently Rowe[3] has published a revision of his diets with tables showing the nutritive value of each, including the content of calcium, phosphorus, iron, and vitamins.

VANDERBILT CLINIC DIETS

In the Allergy Division of the Dermatological Clinic the original Rowe diets have been successfully used in adults, but after a brief experience it appeared that similar diets might be formulated for both children and adults which would preserve the diagnostic value of Rowe's but would be easier to apply in the treatment of clinic patients. These clinic diets have been in use for more than a year and are published with recipes and notes on administration in the hope that they may be of aid to others in carrying out the somewhat difficult procedure of diet testing. In addition to having the clinic elimination diets

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TABLE I

VANDERBILT CLINIC DIETS

	ADULTS				CHILDREN			
	DIET 1	DIET 2	DIET 3	DIET 4	DIET 5 FOR INFANTS	DIET 6 CHILDREN 1-2 YR.	DIET 7 SCHOOL CHILD	DIET 8 SCHOOL CHILD
Beverage	Coffee	Milk Chocolate[d]	Tea Lemonade	Grape juice	Sobee[o]	Sobee Lemonade	Sobee	Lemonade
Fruit	Grapefruit Prunes Plums	Apple Apricots	Peaches Banana Lemon	Grapes Raisins Pears	Grapefruit juice Lemon juice	Lemon juice Banana	Apricots Banana	Apple Lemon
Vegetable	Peas (any kind) Corn (any kind)	Beets Lettuce	Onion Carrots Lentils	Beans (any kind) Turnips (yellow or white)	Carrot String beans	Carrot String beans	Carrot Beans (all kinds)	Corn Beets Peas
Meats	Lamb Mutton	Beef Veal	Mackerel Salmon	Chicken Egg	Lamb	Lamb	Lamb	Beef
Cereal	Corn[a] Hominy	Rice[e] Rye	Wheat[h]	Barley Oatmeal Steel-cut oats	Barley Oatmeal	Barley Oatmeal	Barley Oatmeal	Corn Rice
Bread	Corn pone Corn crisps	Rye-rice muffin Whole rye wafer[f]	Homemade biscuit Whole wheat bread[i] Some wheat crackers[j]	Barley-oatmeal muffin	——	Barley-oatmeal muffin	Barley-oatmeal muffin	Corn pone Corn crisps
Fat	Corn oil[b]	Beef suet Butter or cream	Cotton seed oil[k]	Olive oil Chicken fat	——	Olive oil	Olive oil	Corn oil[b]
Miscellaneous	Corn syrup[c] Plum jam Molasses Molasses candy	Vinegar Cheese Apple butter Chocolate fudge Plain milk-chocolate bars[g] Mineral oil	Spaghetti[l] Peach jam Lemon drops	Olives Grape jelly Peppermint or wintergreen cream candy[n]	Corn syrup[c] Corn sugar Viosterol[p]	Viosterol[p]	Chocolate Apricot jam Chocolate candy (homemade)	Corn syrup[c] Molasses Apple butter

Water, cane sugar, brown sugar, powdered dextrose, salt, gelatin,[m] baking soda, cream of tartar,[s] hard candy,[a] may be used freely on all diets.

Diets 5, 6, and 7 contain practically the same foods but are adapted for different ages. If the mother is unable to bake the prescribed bread substitutes, Ry-Krisps[f] may be added.

[a]Corn meal mush or Post Toasties.

[b]Corn oil, Mazola, manufactured by the Corn Products Refining Co., is stated to contain only pure corn oil.

[c]Corn syrup, Karo, Blue Label, manufactured by Corn Products Refining Co., is stated to be made from 85-90 per cent corn syrup and 10 per cent refiners' sugar.

[d]Chocolate, this applies to a pure chocolate or cocoa and does not indicate chocolate preparations, such as the cocoa malt or chocolate malted milk preparations.

[e]Rice, preferably brown or as Puffed Rice, Quaker Oats Co., or Rice Krispies, Kellogg's.

[f]Ry-Krisps, whole rye wafer stated to be made from whole rye, salt, and water. Manufactured by the Ralston Purina Co., St. Louis, Mo.

[g]Plain Hershey milk chocolate bars are stated to be made from whole milk, chocolate, and sugar. Filled chocolate candy bars or chocolate creams may not be used as they usually contain egg and sometimes nuts or fruits.

[h]Wheat breakfast cereals as Farina, Cream of Wheat, Wheatena, Shredded Wheat, Puffed Wheat, etc.

[i]Whole wheat bread as baked by the leading bakers in New York City is stated to be made without milk. It usually contains yeast and frequently lard which introduces additional foods. Practically all New York white bread does contain milk. This may not apply in every community.

[j]Uneeda Biscuits and Graham Crackers of the National Biscuit Co. are stated to be made without milk or eggs.

[k]Cotton seed oil, i.e., Crisco, manufactured by Procter and Gamble. It may be salted and also used as a very good substitute for butter.

[l]Spaghetti, this does not include macaroni and noodles as some brands of macaroni contain milk and all noodles contain egg.

[m]Commercially prepared lemon flavored gelatin may be used on diets 3, 6, and 8, but on the other diets it is necessary to use unflavored gelatin as the allowed fruit flavors are not prepared commercially.

[n]Hard candy applies to the commercial candy flavored with peppermint, wintergreen, clove, cinnamon, etc., but not to soft candies, such as marshmallows, fondants, creams or nougats because egg white is used in the making of these.

[o]Sobee, manufactured by Mead, Johnson & Co., contains soy bean 67.5 per cent barley flour 9.5 per cent, olive oil 19 per cent, sodium chloride 1.3 per cent and calcium carbonate 2.7 per cent. If it is prepared by using 1 ounce of Sobee to 7 ounces of water, the nutritive value of one fluid ounce is approximately equivalent to 17 calories. The percentage composition in normal dilution is carbohydrate 4.07 per cent, protein 4.15 per cent and fat 2.81 per cent.

[p]Viosterol, irradiated ergosterol usually with corn oil as a vehicle. If corn is contraindicated, suggest using Abbotts' Viosterol which is irradiated ergosterol in sesame oil.

[q]Margarine, vegetable or animal fat churned with milk containing from 4 per cent to 6 per cent milk solids. This applies to such common butter substitutes as oleomargarine and Nucoa.

[r]Malted milk, whole milk and extracts of malted barley and wheat.

[s]Baking soda and cream of tartar are used in place of baking powder because in baking powder the soda and cream of tartar are combined with some starch varying with the brand of powder.

[t]Commercial ice cream almost always contains egg.

of diagnostic and therapeutic help, an effort has been made to have them practical, simple, inexpensive, and adequate. Care has been taken to have the lists mutually exclusive, i.e., to have no possible allergen included in more than one diet. In Rowe's diets several foods such as rice, peas, and pears, are included in more than one diet. This may be confusing if the symptoms become worse and a second diet has to be tried.

Together with most observers we have found that the foods to which allergic patients are most commonly sensitive are egg, milk, wheat, orange, tomato, and cod. The three former are the basis of our daily food intake and yet are the most common allergens. It is unusual for one patient to be sensitive to milk, wheat, and eggs, and it is difficult to arrange practical diets which contain no trace of these foods. Therefore a series of four diets for adults was arranged of which the first contains none of these three foods. Diet No. 2 contains milk but neither egg nor wheat; diet No. 3 wheat but neither milk nor egg; and diet No. 4 egg but neither wheat nor milk. No diet contains orange, tomato, or cod. As shown in Table I each diet is made up of mutually exclusive proteins and contains one or two beverages, two or three vegetables, two or three fruits, one or two cereals, and a meat or two fish. Water, sugar, salt, gelatin, hard candy,[n] cream of tartar, and soda are common to all diets.

As it is easier to find substitutes for the common foods for a child, the four diets for infants and children contain none of the most common allergens. Diets 5 and 6 are for infants and small children and diets 7 and 8 for school children.

As to the adequacy of the diets, meats are used on all to furnish sufficient protein. The carbohydrate is furnished by cereals, bread substitutes, sugar, jam, jelly, and homemade candy. Sweetened fruit juices or hard candies which are flavored with fruit on the particular diet or with oils, such as peppermint or wintergreen, may be used to augment the caloric intake. Fat is present on each diet in the form of oil or butter. The amount of food which the patient may eat is not restricted. The patient is urged to eat plentifully of the prescribed vegetables and fruits to prevent constipation. Salted yellow vaseline which some patients will use as a butter substitute is also useful in this respect. The adult diets, with the exception of diet 2, are somewhat low in minerals but as new foods are usually added within three weeks, the deficiency has not been important. When it is necessary to keep a patient for a long period on these diets, a powder containing equal parts of calcium gluconate, sodium phosphate, and ferrous carbonate might be given with each meal.

On the children's diets with the exception of 8, Sobee,[o] a synthetic food formulated by Hill and Stuart,[4] is using as a milk substitute. The protein of the soy bean which it contains is sufficient to meet the re-

quirements of younger children. It is rich in vitamin B. Minerals are present in adequate amounts. In our experience, even after prolonged use, the growth record of children fed on Sobee compares favorably with the growth of children fed on cow's milk. The only contraindication to its use has been in infants sensitive to barley, one of the ingredients of Sobee.

METHOD OF USING DIETS

The method of employment of these diets for adults or school children is as follows: The patient is placed on one diet for at least a week and frequently for two weeks. If this has no effect on his symptoms, successive diets are tried until one is reasonably certain that the foods each contains either have or have not a definite influence on his symptoms. If a patient becomes worse on one diet, another is substituted. If he becomes definitely better, this diet is adhered to until the patient has improved sufficiently for an exacerbation of symptoms to be observed. Then, using this diet as a basis, one new food is added at four-day intervals, fruits and vegetables being added first, and then meats and cereals. The other common allergens are among the last foods to be added. If one of the new foods causes a return of the symptoms, it is excluded, and no more additions are made until the patient is definitely improved, so that a recurrence of symptoms resulting from any other foods can be noted. Instead of using one diet as a basis, successive diets may be tried, observing the effect of each one on the symptoms. In the latter instance, after each of the four diets have been tried, the ones on which the patient showed definite improvement are combined and prescribed for a week or two. At the end of this time if improvement continues, one new food is added at four-day intervals, until one finds the food or foods which cause a recurrence of symptoms.

In children under two years of age either diet 5 or 6 is used, depending on the age of the patient. These diets contain no common allergen and yet are adequate for a limited period. They are useful if the mother has no knowledge of the sensitizing food and if none of the skin tests is positive. If, however, the mother remembers what foods the child was permitted before and after the onset of symptoms, it is possible to have the infant return to the diet taken before the disease appeared. Some of the foods on diet 5 are gradually substituted for the foods which the infant ingested after the onset of symptoms.

ARRANGEMENT OF MEALS

The menus in Table II are presented as examples of how meals may be devised from foods on the various lists. They may be varied at will so long as the restrictions of the list are not overstepped. For infants it is necessary to individualize the amount and frequency of feedings, and no routine menu could be established for diet 5. Dr.

TABLE II

SUGGESTED MENUS

	DIET 1	DIET 2	DIET 3	DIET 4	DIET 6	DIET 7	DIET 8
Breakfast	Grapefruit or prunes	Apple sauce or stewed apricots	Banana or peaches	Baked or stewed pears	Lemonade	Apricots or banana	Apple, raw, baked, or sauce
	Post Toasties or fried corn meal mush with corn syrup	Puffed rice or Rice Krispies	Farina, Wheatena, Ralston, or Puffed Wheat with syrup from canned peaches or cane syrup	Oatmeal with brown sugar or pear syrup	Oatmeal or barley with brown sugar syrup	Oatmeal or barley with brown sugar syrup	Corn meal mush, Post Toasties or Rice Krispies or Puffed Rice with syrup, sugar or apple sauce
	———	———	———	Eggs (scrambled with olive oil)	———	———	———
	———	Toasted Ry-Krisps with butter	Homemade biscuit with peach jam or whole wheat toast	Barley-oatmeal muffin with grape jelly	Barley-oatmeal muffin	Barley-oatmeal muffin	Corn pone or corn crisps
	Coffee (black)	Hot chocolate or milk	Tea (with lemon if desired)	Grape juice	Sobee	Chocolate Sobee	Lemonade
Lunch	Lamp chop	Beef or veal steak	Canned or broiled salmon	Chicken or eggs	Minced lamb or lamb chop	Lamb chop or roast lamb	Beef steak or roast beef
	———	Boiled rice	———	———	———	———	Rice or hominy
	Peas or corn	Buttered beets	Carrots or onions	String or wax-beans	Carrots or string beans	Carrots or beans (any kind)	Peas, beets, or corn
	———	Lettuce salad with mineral oil dressing	———	Olives	———	———	———
	Plum gelatin	Raw apple or poor man's rice pudding	Banana or peach pie (crust made with Crisco)	Canned pears or grapes	Lemon gelatin or banana	Baked banana or apricots	Lemon gelatin, lemon ice or Indian pudding
	Corn pone or corn crisps	Ry-Krisps	Uneeda biscuits or Graham crackers	Barley-oatmeal muffin with raisins	Barley-oatmeal muffin	Barley-oatmeal muffin	Corn pone or corn crisps
	Grapefruitade	Milk	Tea	———	Sobee	Sobee	Lemonade
	———	———	———	———	———	Chocolate candy	Lemon lollipop or brown sugar candy

TABLE II—CONT'D

	DIET 1	DIET 2	DIET 3	DIET 4	DIET 6	DIET 7	DIET 8
Dinner	———	Beef bouillon or veal consommé	Lentil soup	Chicken broth with barley	Oatmeal or barley or lamb broth with barley	Oatmeal or barley or lamb broth with barley	Corn or rice cereal or beef broth with rice or corn soup
	Roast lamb	Roast beef or veal chop	Baked or broiled mackerel	Broiled or roast chicken	———	———	———
	Boiled hominy grits	———	Spaghetti with fried onions	———	———	———	———
	Peas	Buttered beets	Carrots	Turnips or lima beans	Carrots or string beans	Carrots or beans	Peas or beets
	———	Lettuce and cream cheese salad	———	———	———	———	———
	Grapefruit or Indian pudding	Baked apple with cream, or apricot whip or homemade ice cream	Baked banana, lemon gelatin or lemon ice	Grape gelatin, pears or grapes	Banana	Banana or apricots	Stewed apple or lemon gelatin
	Corn pone or corn crisps	Rye-rice muffin	Homemade biscuit	Barley-oatmeal muffin	Barley-oatmeal muffin	Barley-oatmeal muffin	Corn crisps
	Coffee (black)	Milk	Tea	Grape juice	Sobee	Sobee	Lemonade

Katherine Merritt and other members of the Department of Pediatrics have cooperated in the preparation, from the limited number of foods on this list, of feeding schedules adapted to the age and nutritional requirements of the patients.

MEALS OBTAINABLE AT RESTAURANTS

If it is necessary to obtain all one's meals in a restaurant, Table III will indicate those foods which are procurable. If there is no evidence of milk sensitivity, diet 2 is the most practical diet as it is sometimes difficult to buy cooked food without milk or butter. However, if the patient will specifically state that he wants the food cooked without butter, it is possible to obtain the foods allowed on the other diets in a good restaurant. It is advisable, in some instances, to add Ry-Krisps[f] to diets 1 and 4 as a bread substitute. But this is the only change that will need to be made in order to make the diets practical for the patient who must eat in a restaurant. Candy and sweetened fruit juices (depending on the flavor permitted) will make the meal more satisfying.

TABLE III

RESTAURANT DIETS FOR ADULTS

	DIET 1	DIET 2	DIET 3	DIET 4
Beverage	Coffee	Milk Chocolate Cream	Tea Lemonade	Grape juice
Fruit	Grapefruit Prunes Plums	Apple Apricots	Peaches Banana Lemon	Grapes Raisins Pears
Vegetable	Peas Corn	Beets Lettuce	Onions Carrots	Beans (any kind) Turnips
Meat	Broiled lamb chop (no butter)	Steak (beef) Veal chop	Canned salmon	Eggs (boiled)
Cereal	Corn meal mush Post Toasties Hominy grits	Puffed Rice Rice Krispies Boiled rice	Wheat cereals as Farina, Puffed Wheat, Wheatena, etc.	Oatmeal
Bread substitute		Ry-Krisps	Whole wheat bread Soda or Graham crackers	
Miscellaneous	Plum jam Corn syrup	Vinegar Cheese Apple butter	Peach jam Lemon ice Lemon gelatin	Olives Grape jelly

Water, salt, brown or cane sugar may be used on all diets.

1. Order all vegetables cooked without butter (except on diet 2).
2. Do not order gravies, soups, roasts, or chicken as these are likely to be seasoned with foods not allowed on your diet.
3. Eat the cereal with only sugar or the allowed fruits, syrup or jam.
4. Ry-Krisps on diet 2 will have to be carried with you and used for bread, as not all restaurants carry Ry-Krisps.

COMPOSITION OF COMMON FOODS

One of the reasons for the failure of a diet to relieve allergic symptoms is, that because of the lack of knowledge of the ingredients of some of the common foods, the patient takes small amounts of some of the prohibited proteins. For instance, if milk is excluded then such foods as butter, cheese, ice cream, macaroni,[l] margarine,[q] white bread[i] puddings, cream soups, cake, cookies, malted milk,[r] milk chocolate,[g] waffles, pancakes, any food containing butter as pie crust, or foods fried or seasoned with butter must also be excluded. If a diet excludes eggs, then such foods as mayonnaise, noodles, custards or milk puddings, rolls that are glazed with egg, cake, cookies, soft or filled candies, ice cream,[t] hot breads, chocolate preparations, such as Ovaltine, must be excluded. If wheat is excluded, then all breads, crackers, cakes, and cookies are prohibited because wheat glutenin is required to make these foods; also wheat flour in any form as when used to thicken stews, gravies, or soups, malted milk,[r] spaghetti, macaroni, noodles, wheat breakfast cereals as Ralston, Pettijohns, Farina, Bran, etc., must be excluded. In prescribing cod liver oil for children having an allergic disturbance, one should remember that cod is one of the common allergens. Tomatoes are likely to be in any soup, gravy, or sauce prepared in a restaurant, and in canned products such as soups, pork and beans, and spaghetti. Orange is comparatively easy to avoid, but pure orange flavoring is used in such articles as orange lollipops, jello, etc. These are just a few common instances which show how a patient who thinks he is adhering to the diet may be in reality taking some of the forbidden food in a disguised form.

To aid patients in obtaining foods which conform to the diet rules inquiry has been made of manufacturers as to the ingredients of certain commercial products. An astonishing number of footnotes containing such information has been appended to the diet tables because it has been found essential in the practical application of this diagnostic method.

INSTRUCTION OF PATIENTS

Some of the other difficulties in the carrying out of the diets are the failure of patients to appreciate the importance of strict adherence to a diet. For this reason the following rules have been formulated for clinic patients:

RULES FOR CARRYING OUT YOUR DIET

1. You are being placed on this diet to find out if food causes your skin trouble. It is breaking the diet just as much to take one drop of food not included on your diet as to eat a pound of it.

2. Eat nothing, drink nothing, except the foods specified on your diet.

3. Eat as much as you want of the above foods.

4. The menus are only suggestions. Combine and prepare the foods in any form you desire, as long as you use only the foods included on the list. For instance, if you fry any food, it must be fried only in the fat or oil that is specified on your diet. Add no spices, butter, or vegetables as tomato or onion for seasoning unless they are included in your diet.

5. To prevent constipation:

   a. Drink at least 8 glasses of water a day.

   b. Eat at least 3 or 4 cupfuls of the allowed fruits and vegetables.

CONCLUSIONS

The diets listed have been in routine use in the Allergy Division of the Dermatological Clinic for over a year. The limited number of foods which each contains has made it possible to find a diet on which many multiply sensitive individuals remained free of symptoms. This same restriction in the number of foods and the lack of duplication of proteins in the different diets for adults have made it less difficult to detect the substances responsible for an exacerbation occurring during diet tests. The inclusion of one allergen to which adult patients are often sensitized in diets 2, 3, and 4 has been of diagnostic aid in that patients frequently react when placed on one of these diets after having been for a week or two on diet 1.

The chief advantage of the diets is their practicability. It has been easier to persuade patients to adhere rigidly to these lists and to keep them comfortable and contented during the tests than it has been with other elimination diets which we have tried. Minor changes are necessary in individual cases, but it is believed that these lists will be found useful and practicable in routine clinic use.

The following recipes have proved helpful in the practical application of these diets:

RECIPES FOR DIET 1

Corn Crisps

½ cup corn meal
½ teaspoon salt
1 cup boiling water

Add salt to corn meal. Add boiling water and stir until smooth. Drop from a spoon onto a baking sheet which has been greased with Mazola oil. Cook in hot oven until brown. The crisps should be very thin and small.

Corn Pone

½ cup corn meal
½ teaspoon of salt
½ cup of boiling water

Add salt to corn meal; add boiling water and mix thoroughly. Shape

the dough with the fingers, making oval pones ½ inch thick. Place on baking sheet which has been greased with Mazola oil and cook in hot oven.

Grapefruit Gelatin

1 tablespoon gelatin
¼ cup cold water
½ cup boiling water
1 cup grapefruit juice
¼ cup sugar
pinch salt

Soak gelatin in cold water five minutes and dissolve in boiling water. Add sugar and stir until dissolved; then add salt, grapefruit juice. Pour into mold, first dipped in cold water and chill.

Plum Gelatin

1 teaspoon gelatin
2 tablespoons water (cold)
¼ cup boiling water
¾ cup canned plum juice
pinch salt

Make as grapefruit gelatin.

Indian Pudding

2 tablespoons corn meal
1 cup water
1 tablespoon sugar
1 tablespoon molasses
¼ teaspoon salt
(¼ cup prunes if desired)

Cook corn meal in water in double boiler for twenty minutes. Add molasses, salt, sugar, and prunes. Pour into baking pan which has been greased with Mazola oil. Set pan in a pan of water and bake forty minutes in a slow oven. Serve with Karo syrup.

Grapefruit Drink

3 ounces Karo syrup or dextrose powdered
3 ounces grapefruit juice (about ½ grapefruit)
ice
dash of salt

Heat the Karo slightly so that it will not be quite so thick; or if dextrose is used, mix with a little water and heat until dissolved. Add grapefruit juice and ice. This drink will furnish about 400 calories.

Brown Sugar Candy

1 cup brown sugar
¼ cup water
pinch salt

Mix sugar, water, and salt and cook until it forms a soft ball when dropped in cold water. Remove from fire, cool. Beat until creamy.

RECIPES FOR DIET 2

Poor Man's Rice Pudding

¼ cup rice
1 pint milk
⅓ cup sugar
¼ teaspoon salt

Wash rice. Mix ingredients. Pour into baking dish which has been greased with butter. Cook in slow oven two to three hours. Stir every fifteen minutes during first hour.

Apricot Whip

½ cup whipping cream
4 tablespoons stewed and strained apricots
2 tablespoons sugar
salt

Whip cream, add sugar, salt, and apricots and mix well. This may be served immediately or packed in salt and ice and frozen.

Rye-Rice Muffins

⅓ cup rye flour
⅔ cup rice flour
½ level teaspoon baking soda
¾ level teaspoon cream of tartar
2 teaspoons sugar
⅓ teaspoon salt
⅔ cup milk
1 tablespoon butter

Bake until brown on top (about twenty-five minutes).

Ice Cream

Homemade ice cream made from cream and flavored with chocolate may be used for dessert.

French Dressing Made With Mineral Oil

1 tablespoon vinegar
4 tablespoons mineral oil
½ teaspoon salt
sugar if desired

Mix and beat with egg beater. A dressing of the consistency of mayonnaise may be made by slowly adding the French dressing above to 3 tablespoons of slightly beaten heavy cream.

RECIPES FOR DIET 3

Homemade Biscuits

1 cup flour (wheat)
¾ teaspoon cream of tartar
½ teaspoon baking soda

½ cup water
1½ tablespoons Crisco
¾ teaspoon salt
½ cup water

Mix and sift dry ingredients. Rub in Crisco with two knives or a fork. Add water. May be dropped from spoon onto pan greased with Crisco or may be rolled and cut. Bake in hot oven about twelve or fifteen minutes.

Lemon Gelatin (Individual)

½ teaspoon gelatin
1 tablespoon cold water
1 tablespoon sugar
1½ tablespoons lemon juice
½ cup boiling water
pinch salt

Make as grapefruit gelatin.

Lemon Ice

Lemon ice, commercial lemon ice may be used, as it is stated (by ice cream manufacturers in New York) to contain pure fruit flavor, water, and sugar. This does not include sherbets which contain white of egg.

High Caloric Lemonade—360 Calories

2 ounces glucose
1 ounce sugar
½ cup water
juice of two lemons
dash salt

Cook the sugar and glucose in water until dissolved. Cool, add salt and lemon juice and ice.

RECIPES FOR DIET 4

Barley Oatmeal Muffin

⅔ cup oats or oatmeal
⅓ cup barley flour
1 tablespoon sugar
⅓ teaspoon salt
½ teaspoonful baking soda
¾ teaspoonful cream of tartar
⅓ cup water
1 tablespoon olive oil

Mix in order given. Pour into muffin pans which have been greased with olive oil. Bake in hot oven fifteen to twenty minutes. If muffins are not eaten fresh, it is best to moisten with a little water and reheat in oven before serving. On diet 4 a cookie may be made by adding raisins and more sugar. Drop from spoon onto baking sheet which has been greased with olive oil.

Grape Juice Gelatin

Make the same as lemon gelatin except omit the lemon juice and use ¼ cup grape juice and ¼ cup boiling water instead of ½ cup boiling water.

RECIPES FOR DIET 5

Sobee

1 ounce dry Sobee
7 ounces water
pinch salt

Add water slowly to Sobee and bring to boil. Boil for three minutes. May have sugar added if desired. Serve either hot or cold.

RECIPES FOR DIET 7

Sobee

See diet 5 recipe, to which chocolate may be added as follows: Cook ¾ tablespoon cocoa or chocolate and 1 tablespoon sugar in about 2 ounces of water for ten or fifteen minutes. Then add to regular Sobee recipe. More or less chocolate may be used as desired.

Chocolate Candy

1 cup sugar
½ ounce chocolate
¼ cup water
pinch salt

Melt chocolate, add sugar and water and salt, and cook until it forms a soft ball when dropped in cold water. Remove from fire and cool. Beat until creamy.

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ELIMINATION DIETS AS AN AID IN THE DIAGNOSIS AND TREATMENT OF ECZEMA*

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DIETS

IN A PRECEDING article one of us (I. W.[1]) has described a series of elimination diets which have been in use in the Department of Dermatology of the Vanderbilt Clinic. These have proved of value in the diagnosis of urticaria, asthma, and intestinal allergy, but have been used mainly in the diagnosis and treatment of eczema. The following report is based on our experience in the last-named disease.

FOOD AS A CAUSE OF ECZEMA

There is a wide division of opinion among competent observers concerning the relationship of food sensitization to chronic eczema. However, the observations made in this clinic[4] have forced us to the conclusion that in the majority of cases of infantile eczema, food sensitization is the sole or main exciting cause of the disease. Patients who have had eczema in infancy occasionally suffer from persistent or relapsing eczema during adolescence and early adult life. In many of these adults the food sensitization from which they suffered in infancy persists and may be the sole or a contributing cause of eczema in later years. In others the later eruptions are due to more recently acquired sensitization to contact substances, fungi, or staphylococci, and food seems without influence on their disease.

Clinically eczemas due to food sensitization often resemble closely those due to sensitization to other substances. This and the difficulty in demonstrating the relationship of food to the eruption, especially in cases of multiple sensitization, are probably responsible for the lack of recognition of the causal relationship of foods to these eruptions. It is in this demonstration that the elimination diets described have been particularly useful.

DEMONSTRATION OF SENSITIZATION BY SKIN TESTS

Before the introduction of elimination diets by Rowe[2] clinicians depended chiefly on skin tests for the detection of food sensitization. These have been and still are useful and almost indispensable in the diagnosis of the etiology of eczemas. Evidence of this is the recent development in many dermatological clinics of separate sections for

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the study of allergic skin diseases. These were necessitated by the fact that the elaborate skin tests required could not be performed in the general clinic.

Sensitization to food can often be detected by percutaneous tests with powders obtainable commercially. In many cases, however, the sensitization can only be detected by the intracutaneous injections of extracts and sometimes only by the injection of isolated proteins from foods. Such preparations are not obtainable commercially, and the maintenance of a supply of all the food substances necessary for testing requires a special laboratory. The difficulties encountered in making these tests limit their usefulness in practice.

Two other obstacles should be mentioned. One is that some of these patients are sensitized to food, and such sensitization is revealed by a skin test, although the sensitization bears no relationship to the present symptoms. The obtaining of positive tests which are of questionable clinical significance is often confusing. A still more serious difficulty is the fact that patients will sometimes fail to react on skin tests to a substance which is causing an active eruption, although they will respond typically to such tests after the subsidence of symptoms. This often makes it impossible to detect the causative sensitization by tests during the height of an eruption.

DETECTION OF SENSITIZATION BY DIET

Individuals frequently detect specific sensitization by observing that an exacerbation of symptoms may follow the eating of a certain food. No systematic manner, however, of observing the effect of diet seems to have been developed before the publications by Rowe[2] on his elimination diets. As compared with the food tests these have an advantage in that they require no special equipment or complicated set of reagents and further that they furnish direct evidence that a food sensitivity affects the eruption and not merely that the patient reacts to the food. They demand, however, considerable time and patience and the complete cooperation of the patient. If the patient can receive hospital care and be fed from a diet kitchen the technic is simple, but the rigid exclusion of common food ingredients, such as milk and wheat, presents real difficulties for ambulant patients, especially those of moderate means who attend clinics.

The successful use of the diets requires careful observation. As a rule the feeding of a food to which the patient is sensitized following a period of abstinence provokes a prompt reaction which is quite striking. The chief danger is that such a reaction may be imitated by a simultaneous exposure to some external substance. The improvement following withdrawal of sensitizing substances is less obvious. Abstinence must be persisted in frequently for a week or more before any improvement is noted. Again in patients who are multiply sensitized,

as are most adults with eczemas, one will probably note no visible improvement following the withdrawal of a food which is one causative factor if the patient is taking other foods to which he is sensitized, or if he is also exposed to contact substances to which he reacts, or if the eczema continues to be secondarily infected.

Usually prolonged observation is necessary to secure useful information from the use of diets, and often an exact decision as to the foods causing the eruption cannot be obtained without the assistance of skin tests. Fortunately, if one can succeed in bringing about a remission of the eczema by the use of diets, accurate information can usually be secured by skin tests during such a period of remission. In spite of these drawbacks we believe that it will be found after a trial of dieting and testing that sufficient useful information may be obtained to make the procedure well worth while.

As an illustration of the method of using these diets in eczema the following case history is given. It also shows the possibility of desensitization by the use of a specific peptone (Propeptan Luithlen-Urbach).[3]

T. S., a girl of fourteen years, gave a history of chronic eczema dating from infancy. The areas involved were the neck, antecubital areas, and the hands. The mother had eczema in childhood, one brother asthma, and one sister a mild eczema. As all routine percutaneous and intradermal tests to the ordinary foods and inhalants were negative, the patient was placed on diet 2. She adhered to this diet three weeks and at the end of this time the skin was markedly improved, i.e., all active lesions had disappeared, leaving only areas of lichenification. For the following two weeks diet 1 was added to 2, and the skin remained practically clear. For the next four and one-half months a new food was added to the diet every fourth day. The patient's skin remained clear until wheat was added. On two occasions within twenty-four hours after the ingestion of wheat the patient had a recurrence of eczema in the areas previously involved. Following each exacerbation wheat was excluded from the diet and the skin again cleared. Following this the patient was allowed all foods except wheat and the skin remained clear. Desensitization to wheat was then attempted by the oral administration of wheat peptone. For the past two months the patient remains free from eczema following the ingestion of moderate amounts of wheat.

Tolerance to potato has developed in another patient following treatment with potato peptone.

RESULTS OBTAINED

In order to draw some conclusions as to the value of these diets we have summarized the cases of eczema in which diets and skin tests have been used almost routinely at the Vanderbilt Clinic for more than

a year. The cases have been separated into three groups, the first including those in which we believe the causative factors were first detected by the effect of diets; the second, those cases detected by a positive skin test; and the third, those whose previous experience taught them that specific foods caused an exacerbation of their eczema. We have included all of the 112 patients with chronic eczema as a major symptom for whom at least one of the elimination diets was employed in an effort to determine the effect of food on their disease. A number of these cases have been included in a previous report.[4] Many were observed for too short a time for definite conclusions to be reached, and in others the validity of the test was vitiated by failure to adhere to diets. Among them were several in which it seemed highly improbable from the outset that food was the cause of their disease, but where it was desired to exclude this possibility. These included a few cases of seborrheic dermatitis, lichen chronicus of Vidal, and eczematous lesions occurring in patients with fungus infections.

Sixty-three of the cases were infants or children under seven years. In them the eczema was usually an acute erythemato-vesicular or papular dermatitis involving the face and extremities, but occasionally generalized. In other children the eruption consisted of more chronic patches of papular, infiltrated, and desquamating skin. Characteristic locations were the face, neck, antecubital, and popliteal areas. In some these patches were associated with a mild disseminated papular eczema. In the adults most of the cases in whom causal relationship of food could be demonstrated resembled the more chronic type seen in young children with infiltrated, desquamating, and frequently lichenified areas on the face, neck, and flexures of the elbows and knees, and scattered papular lesions on the arms, trunk, and thighs.

Thirty-six patients who were placed on diets were not sufficiently studied either because they were not followed or because they did not adhere to the diets. The relationship of food to eczema in these patients was recorded in Table I as "undetermined." Food was excluded as a factor in 11 cases, in 7 by means of elimination diets and in 4 who while on diets by either skin reactions or cultures showed that food was not a cause of the eczema.

In the remaining 65 (58 per cent) food was included as a factor in the causation of eczema because the elimination or administration of specific foods caused a change in the patient's eczema. These patients were arranged in three groups. First, where the eczema cleared completely following the elimination of specific foods from the diet, food was considered as the sole exciting cause of the eczema. In this group were 19 patients. The second group included 32 patients who when specific foods were given or withdrawn showed a pronounced exacerbation or regression of eczema but who were not entirely cured when these foods were excluded from the diet. In this group it was felt that food

TABLE I

INFLUENCE OF DIETS ON ECZEMA

RELATIONSHIP OF FOOD TO ECZEMA	NO. OF CASES		RELATIONSHIP OF FOOD DETERMINED BY:					
			(1) ELIMINATION DIETS		(2) SKIN REACTION CONFIRMED BY FEEDING		(3) PATIENTS' OBSERVATION CONFIRMED BY TESTS	
	Under 7	Over 7	Under 7	Over 7	Under 7	Over 7	Under 7	Over 7
Sole exciting cause	15	4	4	3	10	1	1	0
Contributing cause	21	11	15	5	6	5	0	1
Probable cause	7	7	4	2	2	4	1	1
Undetermined	20	16	–	–	–	–	–	–
Excluded	0	11	0	7	–	–	–	–
Total	63	49						

was a contributing cause of the eczema. In the third group the latter conditions also obtained, but the possible influence of ointments or other factors could not be excluded so that food was recorded as a probable cause of eczema. There were 14 in this group.

The striking thing was that of the 63 patients under seven years of age food was demonstrated to be the sole cause of the eruption in fifteen (24 per cent) of the cases and that in an additional twenty-eight (44 per cent) it was shown to be a contributing or probable cause. In no case could its influence be excluded. Of the forty-nine patients over seven years of age food was shown to be the sole exciting factor in four (8 per cent) of the cases and contributing or probable cause in an additional eighteen (37 per cent).

The relative value of skin tests and elimination diets in diagnosis is indicated by comparison of the results obtained in 51 patients in whom food was the sole exciting or contributing cause. Of these the food sensitivity was detected by elimination diets in 27 (53 per cent), by skin tests confirmed by the effect of diet in 22 patients, and by testing with eliminating foods to which the patient had found himself sensitive in two.

Ninety-five per cent of the patients received skin tests (usually percutaneous and intradermal) to foods and other substances before or during the employment of the diets. In spite of this their food sensitivity was in many cases demonstrated only after resorting to the elimination tests.

The 51 patients noted above were found to be predominately sensitive to egg, milk, and wheat, both by skin tests and by diet. Sensitivity also occurred to a variety of other foods. The number of patients who reacted to each food is shown in Table II.

TABLE II

POSITIVE SKIN TESTS OBTAINED IN PATIENTS IN WHICH THESE FOODS WERE THE SOLE EXCITING OR CONTRIBUTING CAUSE*

FOOD	NO. OF TESTS
Egg	21
Milk	13
Wheat	8
Orange	6
Cod	4
Tomato	3

and one positive test to each of the following: barley, buckwheat, corn, rice, plum, grapefruit, strawberry, lamb, tuna fish, potato, spinach, carrot, cucumber, parsnip, and mustard.

*Skin tests were interpreted as positive only when a definite urticarial wheal with pseudopods developed at the test site.

SUMMARY

1. Elimination diets have been found of value in the diagnosis of chronic eczema.

2. As compared with skin tests they present the advantage of: (a) giving direct evidence of the relationship of sensitivity to the patient's symptoms; (b) enabling one to detect sensitivity during the periods when the skin reaction is suppressed; (c) being available to the practitioner when proper reagents for skin testing cannot be obtained.

3. The chief disadvantages are: (a) the difficulty in interpreting results due to the slow response of eczemas to the elimination of foods and to the interference of other sensitizing factors; (b) the tediousness of the procedure; (c) the difficulty of rigidly excluding the most common food allergens from the diet.

4. The combined use of elimination diets and skin tests is usually necessary for accurate diagnosis.

5. Of the 112 patients studied eczema was caused solely by food sensitization in 17 per cent. This sensitivity was determined solely by means of elimination diets in 6 per cent.

6. Desensitization was apparently accomplished in two cases by the use of the specific peptones of Luithlen and Urbach.

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A RATIONAL GROUPING OF THE FOOD ALLERGENS

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VERY soon after Blackley had proved the condition of hay fever to be due to sensitization to specific pollens the idea of sensitization to related pollens seems to have resulted largely through the use of standard botanical nomenclature by those who studied the problem. The use of a standard nomenclature was necessitated by reason of the fact that many popular names are often applied to the same identical plant, and conversely, that the same popular name is often applied to several distinct species. For example, the term "post oak" has been used to designate at least fourteen different species of oak in the United States. The confusion which would arise from discussion of sensitization to "post oak" is obvious.

Although the relationship between the plant foods is quite as obvious as the relationship between the plant germ cells (pollen), it seems to have escaped application until quite recently. This may possibly have been due to the fact that necessity was not so great as in the case of pollens, since popular food names are fairly well standardized.

Some time ago, while going over a paper by Wells and Osborne[1] which records their study of the antigenic relations of purified vegetable proteins, I was led to contemplate upon the apparent lack of clinical application of the idea which their findings suggested. For example, they showed that a guinea pig sensitized to either of certain purified proteins of wheat, rye, or barley could be shocked by either of the other two. Because of the interaction of proteins obtained from barley, wheat and rye they concluded that the specificity of the antigenic substance is determined by the chemical structure of the reacting proteins rather than by their biologic origin.

Notwithstanding the desirability of a classification of antigenic substances on a chemical basis, the present status of protein chemistry precludes any such classification as a possibility. Furthermore a reference to the biologic relationship of the proteins used by Wells and Osborne shows that while the plants from which the proteins were obtained (wheat, barley and rye) were of different genera and species, all are grasses and belong to the same family.

These facts together with the already demonstrated fact that a person sensitive to the pollen of a given species was more often sen-

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sitive to several members of the same family than to those of a different family, induced me to compile a rather complete list of animal as well as plant foods on a toxonomic basis. I then brought together in a tabular form the popular names of the more common foods, as shown in Table III. I found this table very useful in a manner to be described presently and decided to pass the idea on by publishing it. I then became acquainted with the fact that a similar grouping had already been published by Vaughan[2] as a basis for a study on group skin tests. Such differences as exist between the grouping he has proposed and that of my own are of a minor nature and due to differences in nomenclature. The concept of homology has been the dominant idea in both. The grouping I have used contains animal foods in addition to plants.

Since my compilation of the vegetable foods contains several articles that are not included in Table I of Vaughan's paper, I should like to add a supplement to this in order that the list may be made as complete as possible, for some of these are of fairly common use. These additions are shown in Table I of this article.

TABLE I

A BOTANICAL CLASSIFICATION OF EDIBLE PLANTS

(A Supplement to Vaughan's[2] Classification)

COMMON NAME	FAMILY	GENUS	SPECIES
	MONOCOTYLEDONES		
Sorghum	Graminae	Holcus	Sorghum
Leek	Liliaceae	Allium	parrum
Chive	Liliaceae	Allium	schoenoprosum
	DECOTYLEDONES		
Hops	Moraceae	Humulus	lupulus
Hazelnut	Betulaceae	Corylus	americana
Blueberry	Ericaceae	Vaccinium	corymbosum
Dewberry	Rosaceae	Rubus	flagellaris
Tangerine	Rutaceae	Citrus	nobilis
Maple Sugar	Aceraceae	Acer	saccharum
Green and Red Pepper	Solonaceae	Capsicum	frutescens
Ground Cherry	Solonaceae	Physalis	pubescens
Yam	Dioscoreaceae	Dioscorea	Batatas
Dill	Umbelliferae	Anethum	graveolens

In Table II the animal foods are classified according to relationship. It is apparent that in the conventional or culinary classifications of animal foods the principle of homology has been equally neglected as in the plants. Any animal taken from the water has been taken liberties with by being termed a fish.

Grouped under the term "shellfish" one has been accustomed to see lobster, shrimp, oysters and scallops. The first two of these are as far removed in relationship from the last two as are any of the food plants

TABLE II

A SYSTEMATIC CLASSIFICATION OF EDIBLE ANIMALS

	INVERTEBRATA			
	PHYLUM MULLUSCA			
COMMON NAME	CLASS	FAMILY	GENUS	SPECIES
Abalone (red)	Gastropoda	Haliotidae	Haliotis	rufescens
Abalone (green)	Gastropoda	Haliotidae	Haliotis	fulgens
Snail (edible)	Gastropoda	Helicidae	Helix	pomatia
Mussel, salt water	Pelecypoda	Mytilidae	Mytilus	edulis
Mussel, fresh	Pelecypoda	Unionidae	Unio	(several sp.)
Mussel, fresh	Pelecypoda	Unionidae	Anodonta	(several sp.)
Oysters	Pelecypoda	Ostreidae	Ostrea	virginica
Oysters	Pelecypoda	Ostreidae	Ostrea	lurida
Scallops (common)	Pelecypoda	Pectinidae	Pecten	irradians
Scallops	Pelecypoda	Pectinidae	Pecten	islandicus
Scallops (giant)	Pelecypoda	Pectinidae	Pecten	Magellanicus
Clams (soft shell)				
Clams (long clam)	Pelecypoda	Myidae	Mya	arenaria
Clams, razor	Pelecypoda	Solenidae	Eusis	disectus
Clams, razor	Pelecypoda	Solenidae	Eusis	viredis
Clams (hood shell)				
Clams (round)	Pelecypoda	Veneridae	Venus	mercenaria
Squid	Cephalopoda	Loliginidae	Loligo	pealei

TABLE II—CONT'D

PHYLUM ARTHROPODA CLASS—CRUSTACEA			
COMMON NAME	FAMILY	GENUS	SPECIES
Lobster	Nephropidae	Homarus	Americanus
Lobster (European)	Nephropidae	Homarus	homarus
Lobster (Norwegian)	Nephropidae	Nephrops	Norwegini
Lobster (Spanish)		Scyllarides	sculptus
Cray Fish	Astacidae	Astacus	Nigrescens
Cray Fish	Astacidae	Cambarus	Limosus
Shrimp	Crangonidae	Crangon	vulgaris
Shrimp, California	Crangonidae	Crangon	franciscorum
Prawn	Palaemonidae	Palaemon	vulgaris
Prawn	Palaemonidae	Palaemon	serratus
Sou. Shrimp and Prawn	Peneidae	Peneus	setiferus
Spiny Lobster (Florida crayfish)	Palinuridae	Palinurus	argus
Crabs, Rock	Cancridae	Cancer	irroratus
Crabs, Jonah	Cancridae	Cancer	borealis
Crabs, California	Cancridae	Cancer	magister
Crabs, Blue	Portunidae	Callinectes	sapidus
Crabs, Lady	Portunidae	Ovalipes	ocellatus

TABLE II—CONT'D

COMMON NAME	SYNONYM	VERTEBRATA CLASS PISCES FAMILY	GENUS	SPECIES
Anchovy, Western		Engraulidae	Anchovia	delicatissima
Anchovy, California		Engraulidae	Engraulis	mordax
Bass, Black, small mouth		Centrarchidae	Micropterus	dolomieu
Bass, Black, large mouth		Centrarchidae	Micropterus	salmoides
Crappie		Centrarchidae	Pomoxis	annularis
Calico Bass	Strawberry Bass	Centrarchidae	Pomoxis	sparoides
Rock Bass	Goggleeye	Centrarchidae	Ambloplities	rupestris
Bluegill	Blue Sunfish	Centrarchidae	Lepomis	pallidus
Butterfish	Harvestfish	Stromateidae	Pronotus	triacanthus
Harvestfish	Whiting	Stromateidae	Peprilus	paru
Buffalo, common		Catostomidae	Ictiobus	cyprinella
Buffalo, white		Catostomidae	Ictiobus	bubolus
Drum	Lake Carp	Catostomidae	Carpoides	thompsoni
Sucker, common	White sucker	Catostomidae	Catostomas	commersoni
Catfish, blue	Mississippi Cat	Siluridae	Ictalurus	furcatus
Channel Cat	Spotted Cat	Siluridae	Ictalurus	punctatus
Codfish		Gadidae	Gadus	callarias
Haddock		Gadidae	Melanogrammus	aeglefinus
Flounder (Atlantic)		Pleuonectidae	Glyptocephalus	cyanoglossus
Flounder (Atlantic)		Pleuonectidae	Pleuronectes	americanus
Flounder (Pacific)		Pleuonectidae	Platichthys	stellatus
Halibut (Atlantic or Pacific)		Pleuonectidae	Hippoglossus	hippoglossus
Halibut (Pacific)		Pleuonectidae	Paralichthys	californicus
Pike, Wall-eyed	Jack Salmon	Percidae	Stizostedion	vitreum
Pike, Sand	Sauger	Percidae	Stizostedion	canadense
Perch, Yellow	Ringed Perch	Percidae	Perca	flavescens
Pickerel	Common Pike	Esoscidae	Esox	lucius
Muskellunge		Esoscidae	Esox	masquinongy
Herring, common		Clupeidae	Clupeus	larengus
Herring	Calif. Herring	Clupeidae	Clupeus	pallasii
Shad, common		Clupeidae	Alosa	sapidissima

TABLE II—CONT'D

COMMON NAME	SYNONYM	FAMILY	GENUS	SPECIES
Sardines	Spanish Sardine	Clupeidae	Clupanodon	pseudohispanicus
Sardines	Calif. Sardine	Clupeidae	Clupanodon	ceruleus
Smelts, American		Argentinidae	Osmerus	mordaxchthys
Smelts, California		Argentinidae	Osmerus	thaleichthys
Sturgeon, common		Acipenseridae	Acipenser	sturio
Salmon, Pink		Salmonidae	Oncorhynchus	gorbuscha
Salmon, Red	Sockeye Salmon	Salmonidae	Oncorhynchus	nerca
Salmon, Red	Chinook Salmon	Salmonidae	Oncorhynchus	tsacawytscha
Whitefish	Common whitefish	Salmonidae	Coregonus	clupeiformis
Lake Herring	Cisco	Salmonidae	Argyrosomonas	artedi
Bloater	Silver whitefish	Salmonidae	Argyrosomonas	prognathus
Trout	Rainbow trout	Salmonidae	Salmo	irideus
Trout	Speckled trout	Salmonidae	Salvelinus	fontinalis
Lake Trout	Mackinaw trout	Salmonidae	Cristovomer	namayeush
Lake Trout	Siscowet	Salmonidae	Cristovomer	siscowet
Weakfish	Sea trout	Scienidae	Cynoscion	regalis
Mackerel	Common Mackerel	Scombridae	Scombrus	scombrus
Mackerel	Chub Mackerel	Scombridae	Scombrus	japonicus
Tuna Fish		Scombridae	Thunnus	thynnus
Mackerel	Spanish Mackerel	Scombridae	Scomberomoras	maculatus
		CLASS AMPHIBIA		
Frog	Bull Frog	Ranidae	Rana	catesbiana
		CLASS REPTILIA		
Turtle	Troosts Turtle	Testudinidae	Chrysempys	troosti
Turtle	Diamond back terrapin	Testudinidae	Malacoclemnys	palustris

TABLE II—CONT'D

COMMON NAME	ORDER	FAMILY	GENUS	SPECIES
		CLASS AVES		
Chicken		Gallinae	Gallus	domesticus
Turkey		Gallinae	Meleagris	gallopavo—bronze
Turkey		Gallinae	Meleagris	Americana—black
Goose		Anserinae	Anser	anser
Duck			Anas	domestica
Guinea			Nemida	meleagris
Squab		Columbae	Columba	livia
Quail		Perdicidae	Ortyx	Virginiana
Quail, mtn.		Perdicidae	Oreortyx	pictus
Quail, California		Perdicidae	Laphortyx	Californicus
Grouse		Tetraonidae	Tetrae	cupido—prairie chicken
Partridge		Tetraonidae	Bonasa	nubellus
		CLASS MAMMALIA		
Beef	Ungulata	Bovidae	Bos	taurus
Beef (Buffalo)	Ungulata	Bovidae	Bos	bison—buffalo
Beef	Ungulata	Bovidae	Bos	indicus—Indian cattle
Mutton	Ungulata	Bovidae	Ovis	aries
Goat	Ungulata	Bovidae	Capra	?
Reindeer—Caribou	Ungulata	Cervidae	Cervus	tarandus
Rabbit	Rodentia	Leporidae	Lepus	sylvaticus—U. S. cottontail
Rabbit	Rodentia	Leporidae	Lepus	Americanus—American hare
Squirrel	Rodentia	Sciuridae	Sciuris	hudsonicus—red squirrel
Squirrel	Rodentia		Sciuris	carolinensis—gray squirrel
Squirrel	Rodentia		Sciuris	niger—fox squirrel

from the ferns. The lobster and shrimp belong to the *phylum Arthropoda* which furnishes food species from at least eight families. The mussels, oysters, scallops, edible snails, abalone, clams and squid represent as many families of the *phylum Mollusca*. Among the fishes are found such popular names as bass, trout, salmon and others applying to members of different families.

In Table III the popular names of the more common foods have been grouped according to relationship. Mention has already been made of some differences of detail between this grouping and that of Vaughan. A difference will be noted in family names in that *Rosaceae, Pomaceae* and *Drupaceae* are given separate recognition by Vaughan, while in my grouping I have followed the classification of Bailey[4] and these are brought together in a single family, the *Rosaceae*. This is, however, a minor point, for if they are given separate rank as families, then these families are all shown to be related by being included in the same order, the *Rosales*. Another difference is noted in the cranberry and blueberry group. Bailey included these in the genus *Vaccinia* as a member of the family *Ericaceae*. A similar difference is noted in that the *Ribes* (currants and gooseberries) are included in the *Saxifragaceae*. Such differences are dependent upon an incomplete standardization of nomenclature and simply show a lack of agreement in this regard of authoritative sources. Whatever rank the groups are given it will be noted that they contain the same materials.

For convenience Vaughan has used two groups of unrelated substances to which he calls attention. The last group of my table also consists of unrelated substances for the same reason.

I have found this grouping valuable in analyzing the patient's diet, thereby saving much time and material in testing. The patient is asked to check three times those articles eaten frequently (daily or at least several times weekly); twice those eaten occasionally (at least once a week; and once those eaten rarely, or less frequently than once a week.

This analysis serves a purpose similar to a botanical survey of the region of a patient suffering from pollenosis. Every one who has had experience with pollenosis knows that the treatment of the patient must be based upon an interpretation of the botanical survey as well as upon the skin test. Obviously it is needless to inject the extract of a pollen to which the individual is not exposed.

Furthermore a patient may be sensitive to substances to which he gives no positive skin reaction.[3] In these cases, the classification on basis of relationship makes possible the elimination of homologous proteins all at one time and puts the elimination diet on a more rational basis.

CASE 1.—The substances checked in Table III represent the diet of C. K., a graduate student at the University of Minnesota. He has had

TABLE III

THE FOOD GROUPS—CHECKED DIET IN CASE 1

GROUP	GROUP	GROUP	GROUP
1. *Ungulatae*	9. *Mullusca*	18. *Cruciferae*	ROSACEAE
Beef	Clams	Cauliflower	(Family)
Lamb	Oysters	Cabbage xx	27. *Pyrus (Gen.)*
Mutton	Scallops	Turnip	Apple xx
Pork	Abalone	Mustard xx	Pear
Veal		Radish xx	
	10. *Graminae*		ROSACEAE
2. *Milk*	–Wheat xxx	19. *Cruciferae*	28. *Prunus (Gen.)*
±Cow's milk,	Oats	Brussels sprouts	Apricot
whole xxx	Rye	Broccoli	Almond
casein		Kale	Peach xx
lactalbumin	11. *Graminae*	Kohl-rabi	Prune
Goat's milk,	Barley	Watercress	Cherry
whole	Corn	Rutabagas	Plum
casein	Rice		
lactalbumin	Sorghum	20. *Compositae*	ROSACEAE
		–Lettuce xxx	29. *Rubus (Gen.)*
3. *Cheeses*	12. *Umbelliferae*	Endive	Raspberry
American xx	–Carrot xxx	Salsify	(black)
Camembert	Celery		Raspberry
Edam	Dill	21. *Compositae*	(red)
Cheddar	Parsley	Chicory	Blackberry xx
	Parsnip	Dandelion	Strawberry xx
4. *Cheeses*		Artichoke	Strawberry
Gorgonzola	13. *Solonaceae*	Jer. artichoke	(wild)
Limburger	–Potato xxx		
Roquefort	Tomato xx	22. *Chenopodiaceae*	30. *Ericaceae*
Swiss	Eggplant	Beet	Cranberry
	Green pepper	Swiss chard	Blueberry
5. *Eggs (Hen's)*	Red pepper	Spinach	
+Whole egg xxx	Ground cherry		*Saxifragaceae*
Egg white		*Polygonaceae*	Currants
Egg yolk	14. *Leguminosae*	Buckwheat	Gooseberry
	–Beans, lima xxx	Rhubarb	
6. *Aves*	Beans, kidney xx		31. *Rutaceae*
Chicken x	Beans, navy xx	23. *Dioscoreaceae*	Lemon xx
Duck	Beans, string	Yams	Orange x
Goose			Tangerine
Guinea	15. *Leguminosae*	*Convolvulaceae*	Grapefruit x
Squab	–Pea xxx	Sweet potato	
Turkey	Black-eyed pea		32. *Miscellaneous*
	Peanut x	24. *Moraceae*	Grape xx
7. *Pisces*	Lentils	Hops	Pineapple x
Bass		Figs	Banana xx
Crappie	16. *Cucurbitaceae*	Mulberry	–Olive xxx
Pike	Cucumber		
Whitefish	Squash	25. *Juglandaceae*	
Herring	Pumpkin	Walnut, Eng-	
Halibut	Muskmelon x	lish x	
Haddock	Cantaloupe x	Walnut, black x	
Salmon x	Watermelon x	Butternut	
		Hicoria nut	
8. *Crustaceae*	17. *Liliaceae*	Pecan xx	
(Skin tests)	Asparagus		
Lobster	Onion x	26. *Betulaceae*	
Crab	Garlic	Hazelnut	
Shrimp	Leek	Filbert	
Crayfish	Chive	Chestnut	

+ or – before the article indicates skin reaction.

daily attacks of asthma during the past year. It is evident that his diet is very limited. By the group method his diet could be covered in 20 tests. Since the asthmatic attacks were daily in occurrence, it seemed logical that if it were dietary in origin the offending substance was probably consumed daily. A further reference to his diet shows that the required number of tests for those articles checked three times is only nine. Of these egg alone gave a positive reaction. Eggs were excluded from the diet and his asthma disappeared. After a whole month of freedom, eggs were added again and the asthma returned. With subsequent exclusion of eggs it again disappeared.

CASE 2.—F. M., a student, has occasional attacks of urticaria (average of once a week). The offending substance should fall among those checked twice. The total number of tests required for those checked twice are eleven. The number of groups involved are eight. Of the eleven tests two were positive, cabbage and turnips, both of the same group. Other members of the group were not tested but all *cruciferae* were excluded from the diet, and the urticaria disappeared.

These cases are cited to show the value of analysis of the patient's diet on the basis of relationship. The amount of testing is reduced to a minimum. Elimination of related substances is rendered feasible.

Vaughan[2] has shown very definitely that sensitization to several members of a related group is more likely to occur than multiple sensitizations of unrelated substances. Furthermore his investigations show that a patient who gives a group reaction by skin test may have symptoms from a member of the group to which he gives a negative skin test. Obviously the skin test like all other tests in medicine must be correlated and interpreted on the basis of history and clinical trial.

While it is possible that it may later be found that group sensitization is due to a common substance present in related species, such a discovery will only serve to enhance the value of the biologic classification.

The advantages of the biologic classification may be summed up as follows:

1. A complete inventory of the patient's diet in regard to the allergic factor may be done with very little effort and very little time.

2. The inventory saves time in the matter of skin testing, as the causative agents are reduced to the methods of analysis. There is no purpose from the clinical viewpoint, in testing the patient for substances which are not a part of his diet.

3. If group testing is desired, then the mixtures are more likely to give positive results, since the mixtures are more likely to be those of homologous proteins.*

*Protein extracts grouped according to Table III will soon be available from Parke, Davis and Company.

TABLE IV

CHECKED DIET IN CASE 2

GROUP	GROUP	GROUP	GROUP
1. *Ungulatae*	9. *Mollusca*	18. *Cruciferae*	ROSACEAE
Beef xxx	Clams	Cauliflower x	(Family)
Lamb xx	Oysters x	+Cabbage xx	27. *Pyrus (Gen.)*
Mutton	Scallops	+Turnip xx	Apple xxx
–Pork xx	Abalone	Mustard	Pear xxx
Veal x		Radish x	
	10. *Graminae*		ROSACEAE
2. *Milk*	Wheat xxx	19. *Cruciferae*	28. *Prunus (Gen.)*
Cow's milk,	Oats xxx	Brussels sprouts	–Apricot xx
whole xxx	–Rye xx	Broccoli	Almond x
casein		Male	–Peach xx
lactalbumin	11. *Graminae*	Kohl-rabi	–Prune xx
Goat's milk,	Barley x	Watercress	Cherry x
whole	–Corn xx	Rutabagas x	Plum x
casein	Rice xx		
lactalbumin	Sorghum	20. *Compositae*	ROSACEAE
		–Lettuce xx	29. *Rubus (Gen.)*
3. *Cheeses*	12. *Umbelliferae*	Endive	Raspberry
American	Carrot xxx	Salsify	(black)
Camembert	Celery		Raspberry
Edam	Dill	21. *Compositae*	(red) xxx
Cheddar	Parsley	Chicory	Blackberry
	Parsnip x	Dandelion x	Strawberry x
4. *Cheeses*		Artichoke x	Strawberry
Gorgonzola	13. *Solonaceae*	Jer. artichoke x	(wild)
Limburger	Potato xxx		
Roquefort	Tomato xxx	22. *Chenopodiaceae*	30. *Ericaceae*
Swiss	Eggplant	Beet x	–Cranberry xx
	Green pepper	Swiss chard	Blueberry x
5. *Eggs (Hen's)*	Red pepper	–Spinach xx	
Whole egg xxx	Ground cherry		*Saxifragaceae*
Egg white		*Polygonaceae*	Currants x
Egg yolk	14. *Leguminosae*	Buckwheat	Gooseberry x
	Beans, lima x	Rhubarb x	
6. *Aves*	Beans, kidney x		31. *Rutaceae*
Chicken	Beans, navy x	23. *Dioscoreaceae*	Lemon x
Duck	Beans, string x	Yams	Orange xxx
Goose			Tangerine
Guinea	15. *Leguminosae*	*Convolvulaceae*	–Grapefruit xx
Squab	Pea x	Sweet potato x	
Turkey	Black-eyed pea		32. *Miscellaneous*
	Peanut x	24. *Moraceae*	Grape x
7. *Pisces x*	Lentils	Hops	Pineapple x
Bass		Figs x	Banana x
Crappie	16. *Cucurbitaceae*	Mulberry	Olive x
Pike	Cucumber x		
Whitefish	Squash x	25. *Juglandaceae*	
Herring	Pumpkin	Walnut, English	
Halibut	Muskmelon x	Walnut, black	
Haddock	Cantaloupe	Butternut	
Salmon	Watermelon x	Hicoria nut	
		Pecan	
8. *Crustaceae*	17. *Liliaceae*		
Lobster	Asparagus	26. *Betulaceae*	
Crab	Onion xxx	Hazelnut	
Shrimp x	Garlic	Filbert	
Crayfish	Leek	Chestnut	
	Chive		

+ or – before the article indicates skin reaction.

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A COMPARISON OF RAGWEED POLLEN INCIDENCE IN THE UNITED STATES FOR 1929 AND 1930*

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THIS paper is the second chapter in the story of the national atmospheric ragweed pollen study begun in 1929.[1] Credit for the continuation of the study is due to the cooperation of the United States Weather Bureau and the Canadian Meterological Service, without which the survey would have been impossible. Slides were exposed at

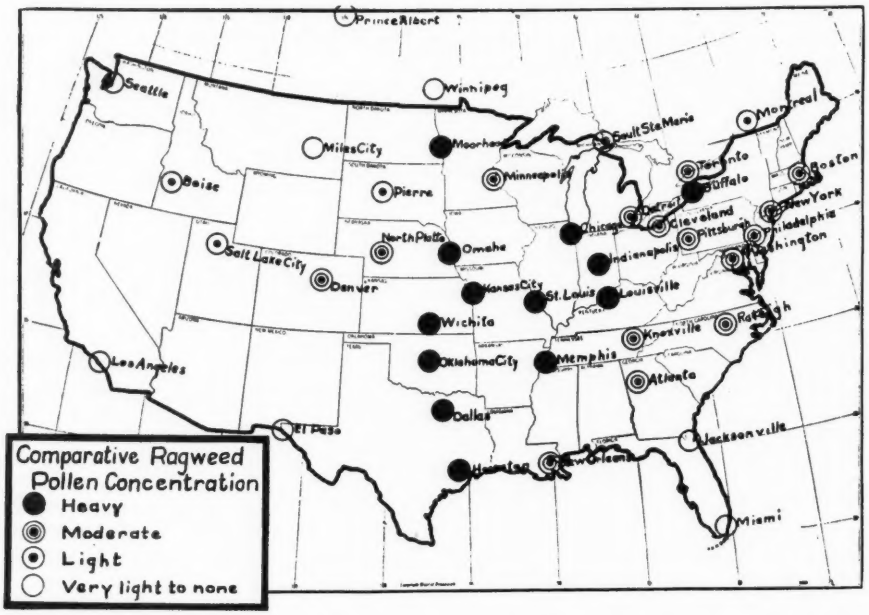


Fig. 1.—The rating shown is based on two years of uniform study in most of the cities. Only United States Weather Bureau stations are used. Numerous local studies in the same and other cities justify these ratings. (Map used by permission of National Map Company, Indianapolis.)

thirty weather stations in the United States and four in Canada. Exposures in a number of cities studied in 1929 were discontinued in 1930 on account of the small amount of pollen found; while a number of new stations were added in an effort to establish a more definite boundary for the ragweed area and to augment the data in important regions. Slides were prepared and exposed in exactly the same way as in 1929. Most of the exposures were made by the same men who had assisted during the previous season, and all counting of slides was done by the same technic[2] and by the same person for both seasons.

*From Biological Laboratories, Swan-Myers Company.

Though a number of stations were added and dropped as noted above, only the twenty-one active stations, at which exposures were made during both seasons, have been considered in the tabulated comparisons, averages and summaries.

OBJECTIVES

The value of atmospheric pollen surveys is becoming more apparent as the work progresses. Several years ago it was seen that certain basic information valuable to hay fever research could be secured by one-season surveys in isolated places. Thus any worker with his own technic of air sampling and counting, and his own method of statement of findings could determine the time and length of the effective ragweed season for his locality and thus have valuable supplemental data to check botanical observations in the field. He could also watch the progress of the season and note the apparent influence of wind and rain on the fluctuations of daily pollen incidence. Soon surveys were begun in a number of localities, and it was evident that a standard technic of air sampling, slide counting and statement of results should be used if results were to be comparable. The uniform nation-wide survey of 1929 produced data which allowed us to sketch the boundaries of the active ragweed region on a "hay fever map." It also enabled us for the first time to study a pollen season from a national viewpoint. Correlation of weather factors and pollen behavior was made possible on a national scale.

Fundamental differences in the ragweed pollen concentration, and in the time and duration of the ragweed season in various parts of the country, brought out by atmospheric studies prior to 1929, were found to be characteristic; and the reasons for these differences, such as latitude, annual rainfall, and agricultural development of a region, were suggested. It is necessary, however, to continue this work over a period of years if adequate investigation is to be made of the causes of the annual fluctuation of pollen incidence. With the compilation of data from the thousands of slides exposed in 1930, new possibilities are brought out. We now have, for the first time, uniform records of two consecutive national ragweed seasons. It is particularly interesting that the second study should come in so unusual a year as 1930 proved to be. The widespread drought resulted in obscuring some of the questions under consideration, but actually simplified others. We are encouraged to believe that we can soon state some general laws concerning ragweed pollen behavior which will lead to a better understanding of a serious medical and economic problem. The study will be continued in 1931.

GENERAL COMPARISONS

A new concept of ragweed pollen as a national "crop" is introduced in this paper. Ragweeds accompany the cultivation of our agricul-

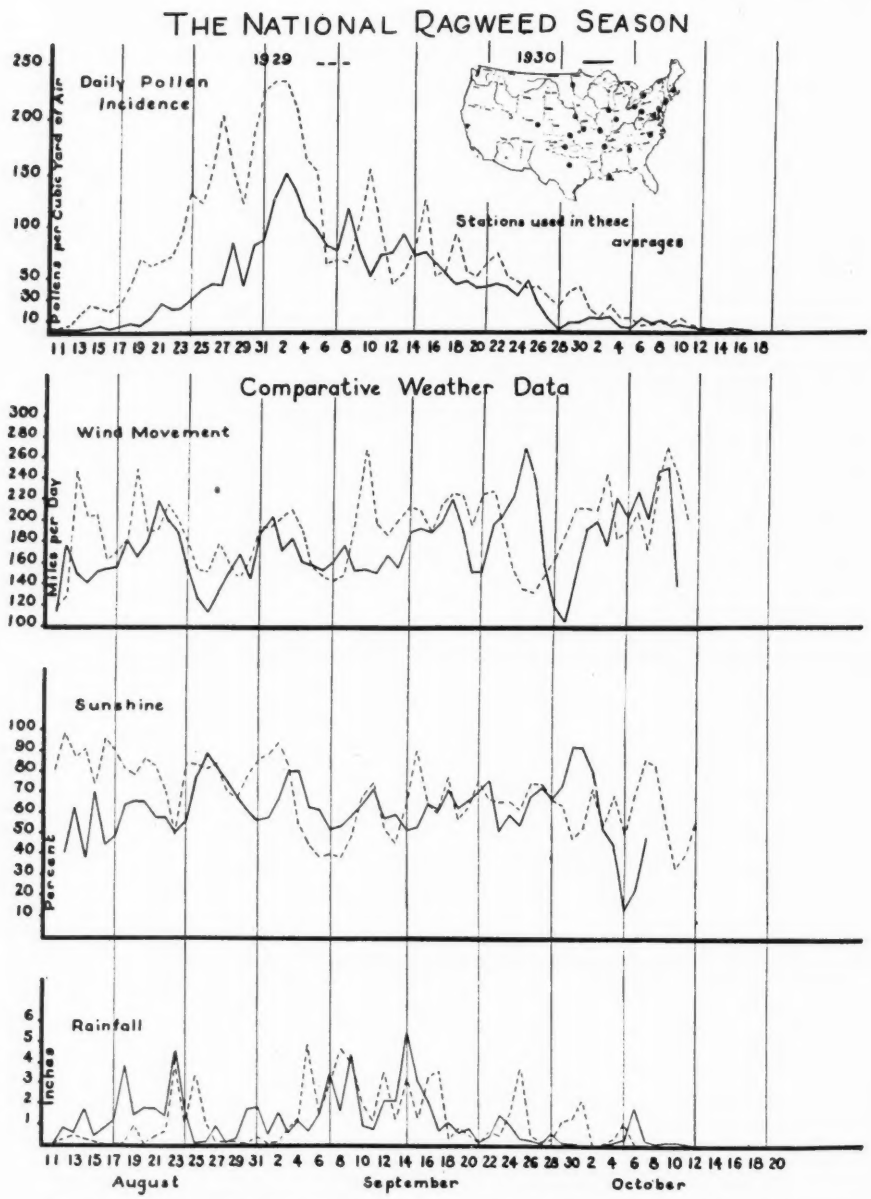


Fig. 2.—All these statistics are daily averages for 21 stations. On this account one can attach considerable significance to any coordination of weather conditions and pollen behavior. A remarkable similarity in the appearances of the first half of the pollen curves for the two seasons will be noticed. A study of the wind, sunshine and rainfall charts will show that this was caused by a remarkable similarity in all weather conditions especially during the last week of August and first week of September. This accidental similarity of form serves to emphasize the great difference in the volume during the first half of the two seasons.

Careful coordinations show that fluctuations in pollen incidence for the two years are caused by the following conditions in the ratio given: Wind 32; sunshine 24; rainfall (interfering) 11.

TABLE I

RAGWEED POLLEN DATA, SEASONS 1929 AND 1930

	LENGTH OF ACTIVE SEASON IN DAYS	AVERAGE DAILY POLLEN CONCENTRATION*		HIGHEST CONCENTRATION*		SEASONAL SLIDE COUNT		
						TOTAL		DEVIATION
		1929	1930	1929	1930	1929	1930	
Eastern								
Montreal†	28		15		79		439	
Boston	26	22	27	82	123	582	707	+21%
New York	31	39	35	128	98	1196	1100	– 8%
Philadelphia	40	45	51	186	242	1799	2040	+13%
Washington	46	43	27	235	132	1956	1241	–36%
Raleigh	35	16	26	69	77	557	929	+67%
Average	34	33	36	140	134	1218	1203	– 1%
Southeastern								
Atlanta	43	33	30	173	126	1437	1284	–11%
Jacksonville†	75		3		18		205	
Great Lakes								
Chicago	35	118	87	466	392	4132	3046	–26%
Detroit†	35		34		194		2193	
Cleveland	35	92	76	460	289	3214	2646	–14%
Pittsburgh	35	71	52	402	173	2499	1828	–27%
Buffalo	35	120	113	565	507	4202	3948	– 6%
Toronto†	35		17		62		581	
Average	35	100	82	473	340	3572	2867	–20%
Central								
Indianapolis	40	286	178	1597	651	11439	7115	–38%
St. Louis	46	124	76	665	492	5686	3487	–38%
Memphis	50	92	60	645	266	4580	2977	–35%
Louisville†	46		86		441		3934	
Knoxville†	41		68		265		2782	
Average	45	167	101	969	470	7235	4526	–37%
Plateau								
Denver	25	71	27	205	67	1767	675	–62%
Salt Lake City†	33		9		25		313	
Plains								
Prince Albert†					5		6	
Winnipeg†	14		9		19		130	
Pierre†	30		13		51		388	
North Platte†	30		24		64		722	
Moorhead	33	190	106	800	427	6267	3501	–44%
Minneapolis†	45		58		208		2596	
Omaha	50	242	76	1241	300	12085	3790	–69%
Kansas City	50	256	81	823	484	12806	4055	–68%
Wichita	59	172	68	738	274	10123	3979	–61%
Oklahoma City	56	113	60	449	334	6309	3360	–47%
Average	49	195	78	810	364	9518	3737	–61%
Southern								
Dallas	54	86	48	605	153	4634	2569	–45%
New Orleans	30	36	66	95	245	1090	1982	+82%
Houston†	46		115		923		5278	
Grand Average	41	108	65	506	279	4684	2679	–43%

*Number of pollens per cubic yard of air.
†Not included in averages.

TABLE II

METEOROLOGIC FACTORS AFFECTING RAGWEED POLLEN PRODUCTION AND DISTRIBUTION DURING 1929 AND 1930

	WIND				TEMPERATURE MEAN DEGREES F.*		SUNSHINE MEAN PER CENT*		RAINFALL IN INCHES		
	TOTAL MOVEMENT, MILES		AVERAGE DAILY MOVEMENT, MILES						DURING JUNE, JULY AND AUGUST		DEPARTURE FROM NORMAL
	1929	1930	1929	1930	1929	1930	1929	1930	1929	1930	1930
Eastern											
Montreal†						65				11.5	+0.11
Boston	3835	3489	147	134	70	69	60	72	5.9	8.63	–1.3
New York	8735	7126	281	230	73	72	68	64	4.7	11.53	–0.8
Philadelphia	10439	8659	261	216	71	71	66	65	7.5	10.53	–1.5
Washington	4546	4106	99	90	71	76	68	68	10.0	6.11	–6.7
Raleigh	5011	4684	143	134	71	77	56	65	13.9	11.43	–3.9
Average	6513	5613	184	161	71	73	64	67	8.4	9.65	–2.8
Southeastern											
Atlanta	8617	5574	200	130	71	75	58	57	7.5	3.88	–9.0
Jacksonville†											
Great Lakes											
Chicago	7367	6076	210	174	68	70	70	74	10.6	6.29	–3.5
Detroit†		6186		177		70		63		4.1	–5.6
Cleveland	8946	7893	257	228	68	69	68	63	12.6	4.51	–4.4
Pittsburgh	5640	4849	160	138	69	71	65	46	7.5	5.84	–6.2
Buffalo	10724	8795	306	251	66	65	67	71	4.5	5.75	–3.4
Toronto†		5456		156		66				6.42	–2.06
Average	8169	6903	233	198	68	69	66	61	8.8	5.6	–4.0
Central											
Indianapolis	7099	7311	177	183	70	71	75	58	13.3	4.53	–5.74
St. Louis	9521	9770	207	213	69	75	65	51	9.7	3.16	–6.6
Memphis	5876	6732	117	135	77	77	66	75	11.8	0.82	–9.3
Louisville†		7817		170		71		63		3.22	–7.6
Knoxville†		3902		95		76		58		6.49	–5.9
Average	7498	7937	167	177	72	74	69	62	11.6	2.84	–7.2

TABLE II—CONT'D

	WIND				TEMPERATURE MEAN DEGREES F.*		SUNSHINE MEAN PER CENT*		RAINFALL IN INCHES		
	TOTAL MOVEMENT, MILES		AVERAGE DAILY MOVEMENT, MILES						DURING JUNE, JULY AND AUGUST		DEPARTURE FROM NORMAL
	1929	1930	1929	1930	1929	1930	1929	1930	1929	1930	1930
Plateau											
Denver	3504	3243	140	130	73	69	69	57	5.0	3.95	–0.5
Salt Lake City†		5404		164		71		81		3.03	+0.7
Plains											
Prince Albert†						65				7.74	+0.06
Winnipeg†						69				8.74	–0.3
Pierre†		5344		178		68				4.64	–3.1
North Platte†		3331		111		71		77		6.38	–2.0
Moorhead	5207	5085	158	151	70	68	82	69	2.0	4.1	–6.4
Minneapolis†		9264		206		69		70		8.32	–2.7
Omaha	7715	6204	154	120	68	70	69	56	9.5	8.87	–2.3
Kansas City	9240	8438	185	169	72	74	72	80	12.8	8.65	–4.5
Wichita	13960	14132	236	240	74	74	64	73	15.5	6.38	–4.5
Oklahoma City	9756	10266	174	183	75	75	71	68	5.9	12.48‡	+3.0
Average	9176	8825	181	179	72	71	72	69	9.1	8.1	–4.1
Southern											
Dallas	12028	12137	223	225	77	76	77	66	0.9	1.52	–8.0
New Orleans	4277	4029	142	134	76	76	71	49	21.5	16.87	–0.6
Houston†		13710		300		81		64		4.06	–8.7
Grand Average	7716	7076	188	172	71	72	68	64	9.15	6.9	–4.0
Deviation from 1929		–8%								–24%	

*During active pollen season.
†Not included in averages.
‡More than half of this amount fell during thirteen hours on June 14 and 15.

tural lands and are subject to the same influences of climate and weather during both the growing and the harvest seasons as are the ordinary field crops. The 1930 ragweed pollen crop was only 57 per cent of that of 1929 (Table I). A large part of the 43 per cent shortage occurred during August and the first week of September (Fig. 2). Since this period corresponds exactly with the season of pollen production of giant ragweed, which matures on the average about two weeks earlier than short ragweed, it is certain that a large share of the shortage must have been due to a lack of giant ragweed pollen. It is important, then, to determine whether the plants failed to produce the usual crop of pollen or whether it was produced and not distributed. It is well known that giant ragweed requires much more moisture than short ragweed. The severe general drought of 1930 came at the critical time for the maturity of giant ragweed, but apparently did not seriously affect short ragweed. Careful field observations as well as the results of pollen collection in the drought area show that this was true. In many places large patches of giant ragweed were left without sufficient moisture by the drying up of creeks and swamps, resulting in arrested development of the plants and the actual death of the unripe flowering tops. A study of Fig. 2 and Table II will show that while wind velocities were lower in 1930 than in 1929, the difference was not sufficient to account for the substantial shortage of the pollen crop. Thus production of giant ragweed pollen was much curtailed while short ragweed was only slightly damaged. A period of local rains about the middle of August came too late to benefit giant ragweed and probably interfered slightly with its pollination. These rains seemed to be almost sufficient for short ragweed.

The corn crop may be used as a practical index of the ragweed crop. Ragweed seems to need about the same climatic conditions for development as corn. The corn belt is the ragweed belt. The amount of rainfall in the summer months determines the yield of corn as well as of ragweed. The 1930 drought with a 24 per cent decrease in summer rainfall in the cities included in the study (a cross-section of the corn belt) was evidently responsible for a 22 per cent decrease in corn production in the United States compared with 1929.[3] This figure tallies very well with the herein estimated 43 per cent shortage in the ragweed pollen crop. Careful correlations indicate that July rainfall is the most important single factor influencing the ragweed crop.

DETAILED COMMENTS

The Great Lakes have been regarded as a natural northern boundary of the ragweed area. To learn something of the severity of the ragweed season in Canada, two series of exposures were made in eastern and two in central Canada. The curves for Montreal and Toronto present true short ragweed studies. No giant ragweed is found in

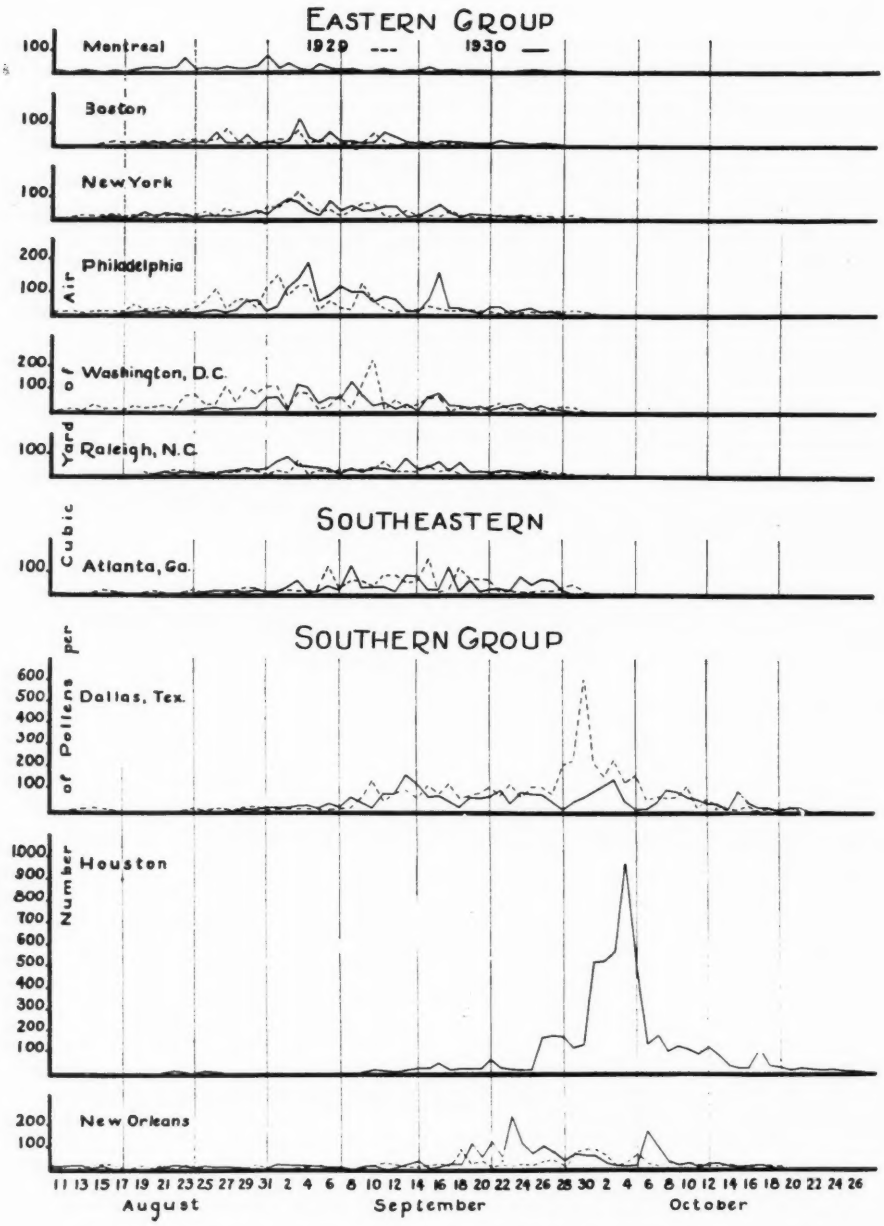
these localities, although it occurs in the southwestern part of Ontario. All agricultural districts of southern Toronto and Quebec probably have a toxic concentration of ragweed pollen, although the season is early and brief.

In view of the vast amount of ragweed which matures after harvest on wheat fields in the United States, it was thought advisable to make investigations of ragweed incidence in the wheat region of Canada, so stations were established at Winnipeg and Prince Albert. The short growing season there as shown by the late maturing of the wheat crop is evidently not sufficient for ragweed. The amount of pollen encountered at Winnipeg was surprisingly small considering its proximity to the ragweed area of North Dakota and Minnesota. At Winnipeg ragweeds mature earlier and the season is more brief than in any district studied so far. If the 1930 results are typical, we may conclude that the edge of the ragweed belt in this part of North America is not far from the Canadian line. In the eastern half of Canada ragweed is not rated as a very prevalent weed.[4]

It was stated in the previous study that Denver marks the western edge of the ragweed area. This was confirmed by exposures at Salt Lake City, where only a comparatively small amount of pollen was found. Ragweed pollen concentration seems to be determined more by rainfall than by topography, as the figures for Pierre and North Platte are much lower than those for Moorhead and Omaha.

Since the results were negative in Miama for 1929, the station was discontinued and Jacksonville substituted in this study. A total of only 205 pollen granules was found on the Jacksonville slides, and these were scattered over two and one-half months. It would seem safe now, in drawing the national ragweed hay fever map, to leave out the Florida peninsula.

Eastern Group (Fig. 3).—Summer rainfall in the cities of our eastern group, with the exception of Washington, D. C., was almost normal in 1930, and although there was less wind movement, the average pollen incidence was almost exactly the same for both seasons. Boston had more rain during the summer and more favorable weather at the season of maturity than it had the year before. Thus with even less wind movement, Boston showed a substantial increase in pollen concentration. Lack of moisture seems almost to have obliterated giant ragweed in the vicinity of Washington. This made the season there at least two weeks late in its onset, although its apex and termination were practically the same as in 1929. Raleigh did not suffer as severely from the drought as some localities. Although the figures on Table II show that this city had less wind movement in 1930, actually it had 20 per cent more wind during the apex of the season than the previous year. This is a good example of the effect of favorable distribution conditions at the peak of the season.



Figs. 3, 4, 5, and 6.—Atmospheric ragweed pollen incidence for 1929, 1930.

Southeastern Group (Fig. 3).—The figures for Atlanta are 11 per cent short of those for 1929. Even this amount is surprisingly high in view of the prolonged drought which affected this part of the South.

Southern Group (Fig. 3).—Dallas may best be compared with the cities in the Plains group where it really belongs on account of its weather conditions. Its only point of comparison with New Orleans and Houston is its tardy and extended season. Dallas' 45 per cent pollen shortage must be due to the same factors which caused even heavier shortages in the cities directly north of it. New Orleans shows the largest increase of any city studied. From the amount of pollen found at Houston it would seem advisable to extend the survey into southern Texas next season.

Great Lakes Group (Fig. 4).—This area shows a 20 per cent decrease in the 1930 pollen crop compared with the previous season. With one exception the cities in this group had less rain during the period of ragweed growth than in 1929 and all of them had less wind movement during the season of pollination. Pittsburgh had the greatest shortage in rainfall and the greatest shortage in pollen incidence, while Buffalo, with slightly more rain than in 1929, had only slightly less pollen than the previous year. That it had any shortage at all must be accounted for by an 18 per cent drop in wind movement during the active season of pollination. Wind direction played an important part in the deficiency of the 1930 pollen crop in Chicago. There was considerably more northeast wind (off Lake Michigan) than in 1929. A most interesting situation is presented by a comparison of the results from Toronto and Buffalo. It will be noted that with the exception of September 2 when Toronto received a heavy rain, the correlation of fluctuation in the two is almost perfect, but that the total pollen found in Toronto is only one-seventh of that of Buffalo. The cities are only 60 miles apart, so conditions of plant growth cannot differ greatly. It is true that there is no giant ragweed in Toronto, which fact must partially account for its low pollen record, but the greatest apparent reason for the low figures is the fact that during the day (when the maximum distribution of pollen takes place) prevailing winds are off the lake, while at Buffalo prevailing winds are from the southwest.

Plateau Group (Fig. 4).—As all the plateau cities used in 1929 except Denver were discontinued, the record of Denver can be compared only with that of the previous season, and with the Salt Lake City figures. At Denver all factors, both for production and distribution, were less favorable in 1930, and the curve is strikingly low.

Central Group (Fig. 5).—The three cities used for comparison in this group show nearly the same percentage of shortage in the figures for 1930. Memphis had almost no rain during June, July and August. The only explanation of its having even two-thirds as much pollen as in 1929 must be the 15 per cent increase in wind movement during the

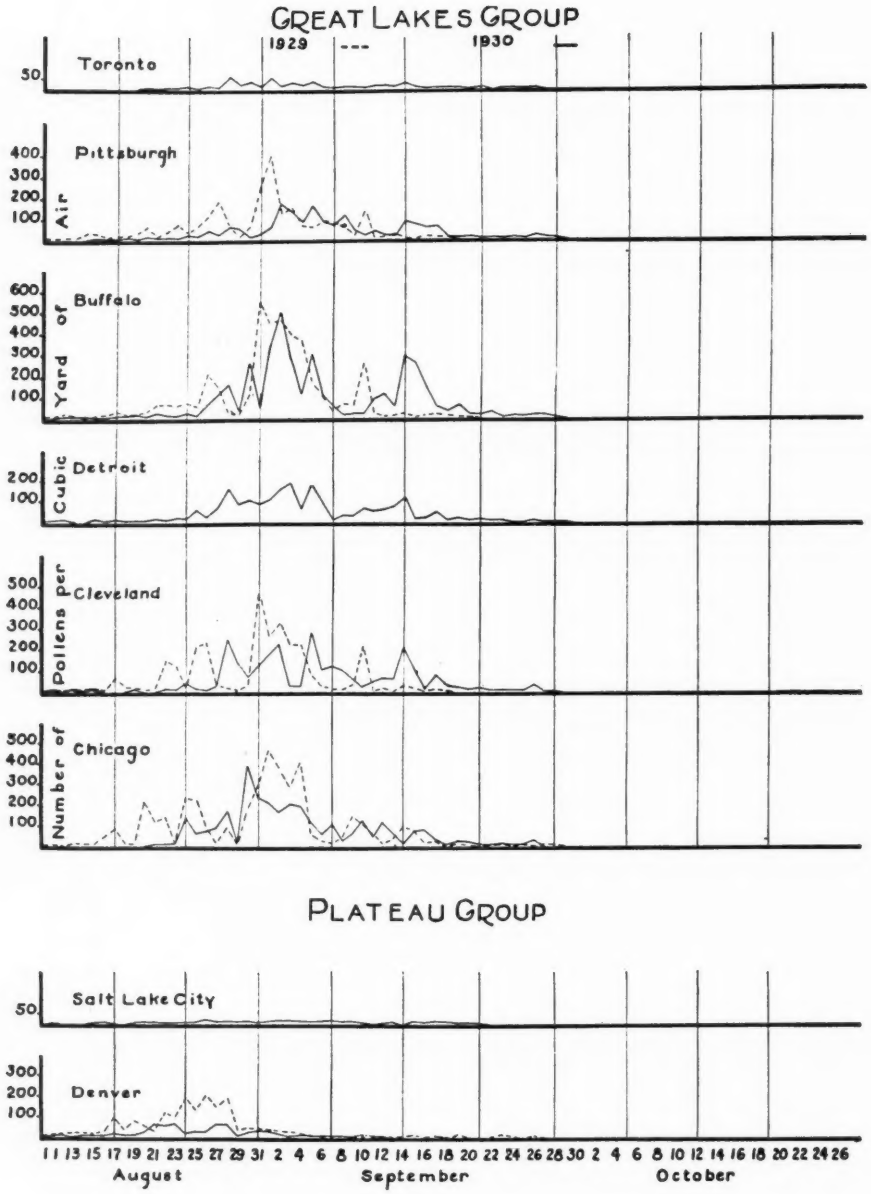

GREAT LAKES GROUP
1929
1930
Toronto
50
Pittsburgh
400
300
200
100
Air
Buffalo
600
500
400
300
200
100
Yard of
Detroit
200
100
Cubic
Cleveland
500
400
300
200
100
Pollens per
Chicago
500
400
300
200
100
Number of
PLATEAU GROUP
Salt Lake City
50
Denver
300
200
100
11 13 15 17 19 21 23 25 27 29 31 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 2 4 6 8 10 12 14 16 18 20 22 24 26
August
September
October

Fig. 4.

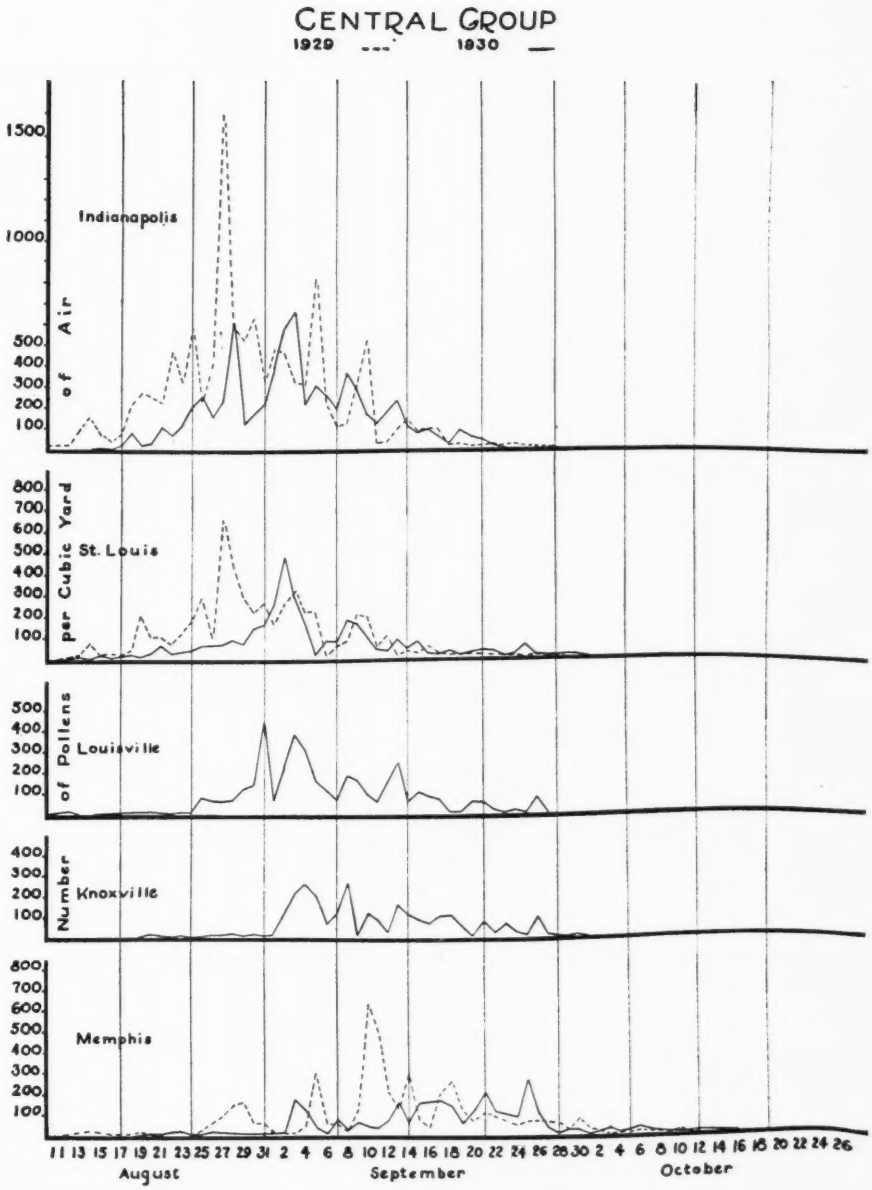

CENTRAL GROUP
1929 ---- 1930 —
Indianapolis
St. Louis
Louisville
Knoxville
Memphis
Number of Pollens per Cubic Yard of Air
August
September
October

Fig. 5

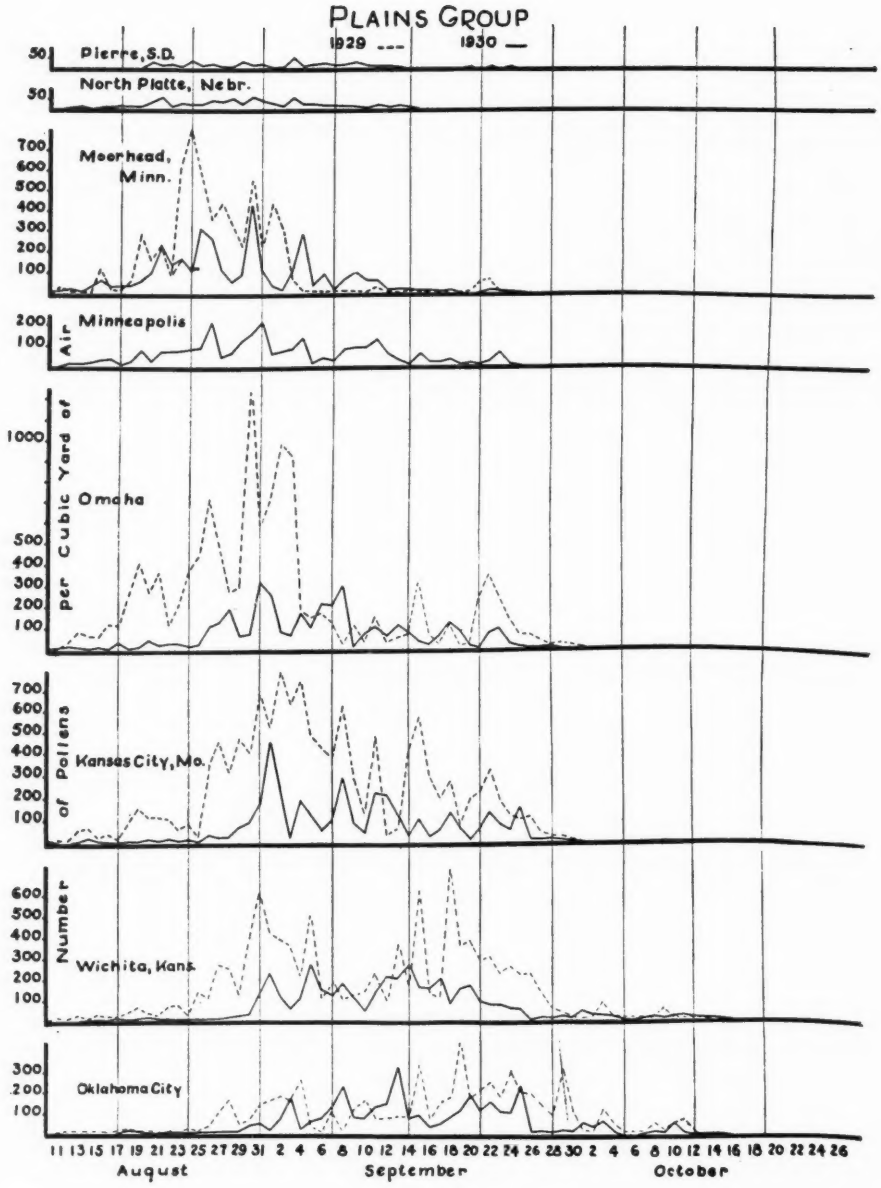

PLAINS GROUP
1929 ---
1930 —
Pierre, S.D.
North Platte, Nebr.
Moorhead, Minn.
Minneapolis
Omaha
Kansas City, Mo.
Wichita, Kans.
Oklahoma City
Number of Pollens per Cubic Yard of Air
August
September
October

Fig. 6.

time of ragweed pollination. It must be noted, however, that all these cities experienced an increased wind movement in 1930. Thus distribution was aided, and the total result was not as low as might have been expected in view of the severity of the drought.

Plains Group (Fig. 6).—In this row of cities west of the Mississippi, the shortage of pollen in 1930 is the greatest of any of the groups, although average figures for the weather factors do not seem to account for so great a difference.

Giant ragweed was greatly damaged at Omaha, Kansas City and Wichita. Whereas the season usually starts in these cities about August 15, they had almost no pollen in the air in 1930 until the first of September. The greatest deficiency of rainfall in these cities was during June and July.

Oklahoma City rainfall figures (Table II) are misleading. While the summer precipitation was twelve inches, more than half of this amount fell in thirteen consecutive hours on June 14 and 15. Thus the effective rainfall was only about half of that given by the official record. Oklahoma City really was much affected by the drought. The corn crop in Oklahoma County (in which Oklahoma City is located) was almost 50 per cent less than in 1929.

CONCLUSIONS

1. A northern boundary of the effective ragweed area is suggested. This includes the agricultural districts of Quebec and Toronto but very little of Central Canada.

2. Low pollen concentration in Toronto is accounted for by the phenomenon of "land and sea" breezes.

3. Florida is practically ragweed pollen free.

4. The severe drought of 1930 reduced the United States ragweed pollen crop 43 per cent below the figures for 1929.

5. July seems to be the critical month for the development of ragweed.

6. The greatest effect of the drought was on giant ragweed.

7. Apparently the weather factors that produce a poor corn crop likewise produce a poor ragweed crop.

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BOTANIC SURVEY OF NEEDLES, CALIFORNIA

With Special Reference to the Hay Fever Producing Flora*

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AS EARLY as 1873, Blackley made various tests with the pollen of certain plants and demonstrated that it could be carried great distances by the wind. Subsequently many studies have been made of this problem, and today hay fever is generally admitted to be a condition of hypersensitiveness to the pollen of a limited group of plants. Although roses, goldenrod, dandelion and other insect pollinated plants may at times be a factor, for practical purposes these may be disregarded and most of the emphasis placed upon wind pollinated plants. This group is characterized by a pollen which is small, light and dry so that it may be easily carried for miles by the wind. These criteria are not the only ones to consider in relation to the hay fever patient. In addition these plants must produce pollen in sufficient quantity to give the air a significant pollen concentration, and most important of all the pollen must be toxic to the allergic individual. It is evident, therefore, that only by a knowledge of the significant hay fever plants, their season of pollination, and relative importance, can one hope to treat the condition successfully and intelligently.

Needles, California, has a population of approximately 4,000 people and is an important division point of the Santa Fe Railroad. Many patients from this town have applied for treatment in the Allergy Clinic. In view of the fact that we were unable to find any detailed study covering this section, it was necessary to make a botanic survey to determine the important offenders and their season of pollination. We hope that the results of our study of this rather isolated area will serve to emphasize to anyone treating allergic patients the urgent need for a comprehensive survey of each district from which patients are drawn.

Three visits were made to this area in an effort to include each of the possible hay fever seasons. The first was made in February, the beginning of the tree season, the next in April, and the final visit in September when the summer-fall season was at its height. In making the primary survey the general type of vegetation and its extent were studied; thus it was possible to make a species list and to choose the sections for intensive study. In September each of the seven sections was studied by the accepted ecologic methods,[1, 2] that is, quadrants and

*From the Allergy Clinic, Santa Fe Coast Lines, Hospital Association.

belt and line transects were made of representative portions to determine the abundance and relative importance of species. From these a complete species list was compiled. Photographs and notes on pollination were taken, and specimens of each species collected and identified.[3] Observations were also made of the abundance and buoyancy of the pollens.

Because the topographic, edaphic and climatic factors of an area condition the distribution of species and are of importance in determining their allergic significance, they will be briefly considered in this report.

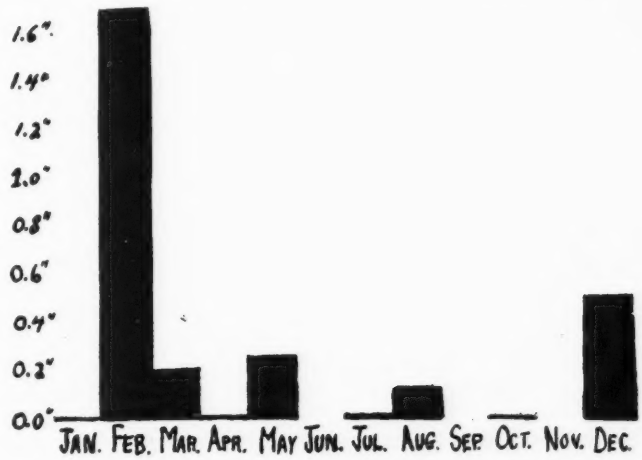

Fig. 1.—Graph of total rainfall during 1928.

Fig. 2.—Graph of total rainfall during 1929.

Needles, with an elevation of 467 feet, is situated in the Mojave Valley on the banks of the Colorado River. The valley is bounded on the south and west by the Mojave and Sacramento Mountains, and on the east by the Black Mountains. The town is about one mile square and is defined by the Colorado River on the north and by small rolling hills on the south. The rainfall of this area for 1928 and 1929 (Figs. 1 and 2) is shown to be typical of a semiarid climate. The rainfall is not only very light but continues throughout all seasons, with the possible exception of the late fall, and shows marked variations from year to year. The temperature (Fig. 3), very high and with no sudden changes, is in keeping with this type of climate.

These factors limit the natural vegetation to that of the semiarid type except along the river where the underground water is more abundant. The warm dry condition is conducive to wind pollinated

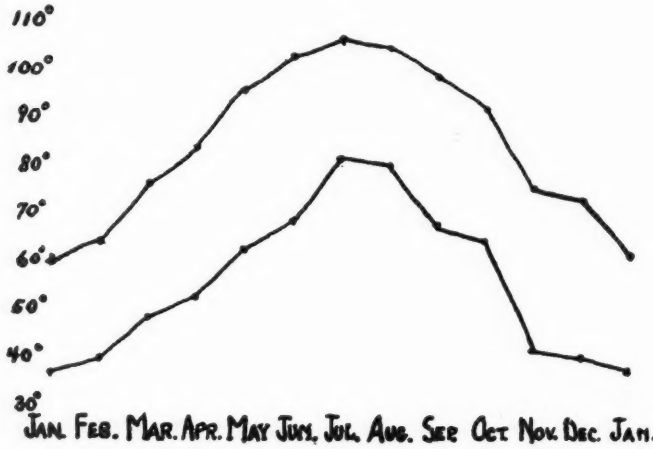

Fig. 3.—Graph of the average maximum and minimum temperatures for 1929.

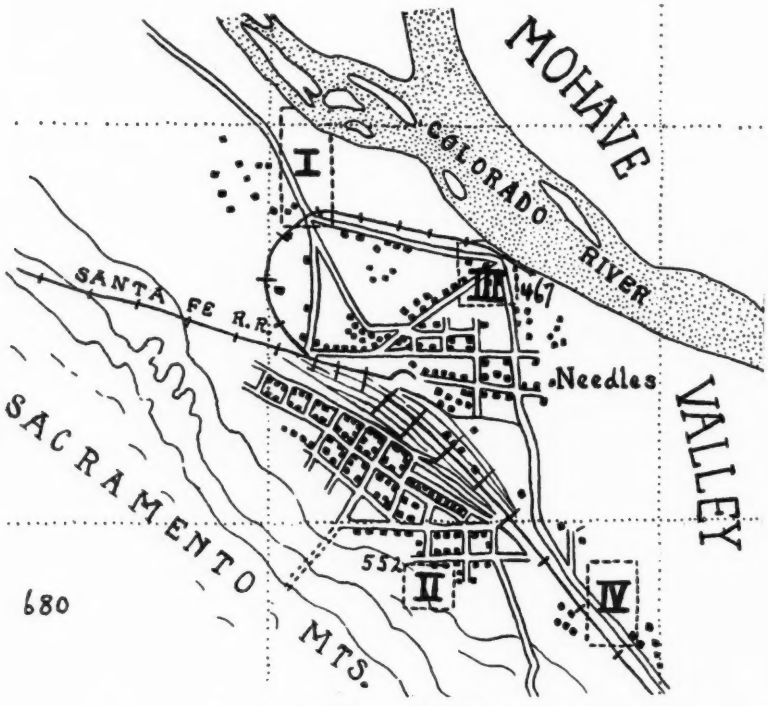

Fig. 4.—Map of Needles, California.

plants. Not one crop of weeds but many are started throughout the summer and fall by the recurring rains and the favorable high temperatures, thus making the pollination season very long and productive.

It is very evident, from the rain and temperature charts, that studies of the abundance or the time and duration of pollination for any one year would be of little value the following year. In addition the heavy winter rains one year and heavy summer rains another will vary the occurrence of species. On the outskirts of the town the soil is quite saline, giving rise to a luxuriant growth of saltbushes and other "salt-loving"[3] plants. Along the river, however, the soil is less saline and the vegetation varies accordingly.

The areas selected for intensive study are indicated on the map in Fig. 4 by roman numerals and will be described in succeeding paragraphs.

AREA I. This is about one-half mile from the center of town. On one side it is bordered by the river and on the other by a dyke, used to

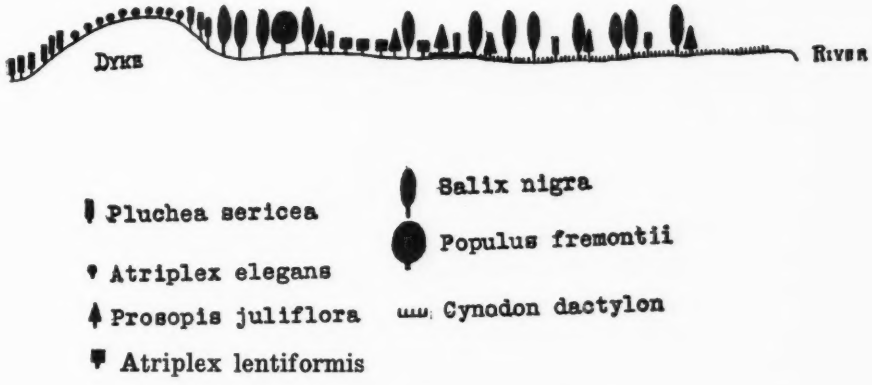

Fig. 5.—Line transect taken Area I.

protect the town from floods. Between the dyke and the river is a meadow approximately 200 feet in width, which continues for a mile or more along the river.

Fig. 5 shows a line transect of this striking community. Just south of the dyke there is a thick growth dominated by *Pluchea sericea.* Progressing toward the river, the dyke is found to be covered with a pure community of *Atriplex elegans,* which is entirely confined to this location. On the north side of the dyke is a compact stand of willows *(Salix nigra)* among which are a few cottonwoods *(Populus fremontii)* and several mesquites *(Prosopis juliflora var. glandulosa* and *var. pubescens).* Beyond this *Salix nigra* continues less abundantly to the river's edge. Scattered throughout is an occasional *Prosopis juliflora* or *Pluchea sericea.* In striking contrast to the typical desert shrub vegetation of the opposite side of the dyke, the whole floor of this meadow is covered with a very luxuriant growth of *Cynodon dactylon.*

In summarizing this area we have:

FAMILY		SPECIES		OCCURRENCE
SCIENTIFIC NAME	COMMON NAME	SCIENTIFIC NAME	COMMON NAME	
SALICACEAE	Willow Family	*Salix nigra*	black willow	abundant
		Populus fremontii	Fremont poplar	occasional
GRAMINEAE	Grass Family	*Cynodon dactylon*	Bermuda grass	abundant
		Typha spp.	cat-tail	rare
CHENOPODIACEAE	Saltbush Family	*Atriplex elegans*		common
		Atriplex lentiformis	lenscale	frequent
LEGUMINOSAE	Pea Family	*Prosopis juliflora vars.*	mesquite	occasional
COMPOSITAE	Sunflower Family	*Pluchea sericea*	arrow-weed	abundant

AREA II. The location of this section is one-half mile south of town. Here the small rolling hills of the Sacramento Mountains begin, giving

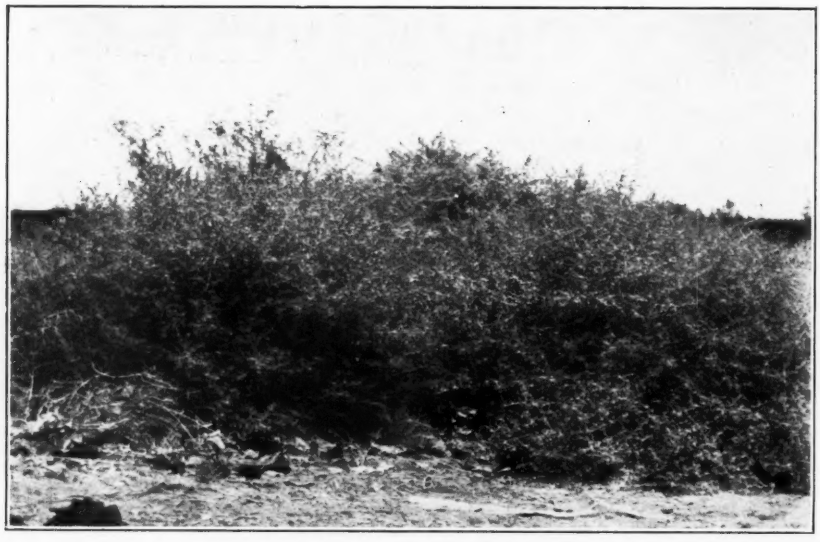

Fig. 6.—Compact stand of *Atriplex lentiformis.*

this area an elevation of 552 feet. Lacking, as it does, an abundant supply of water this location has a typical desert type of vegetation. It is well spaced, with the greasewood, *Larrea tridentata var. glutinosa,* dominating. Scattered throughout were a few *Eremocarpus setigerus,* many *Atriplex polycarpa* and an occasional *Acacia greggii.* The only significant hay fever plant in this area is the cattle spinach (*Atriplex polycarpa).*

AREA III. This section is located about one-half mile from town. Although very near the river it is separated from it by the dyke. Apparently the drainage in this area is very poor, producing a saline soil, in many places forming large crusts on the surface. Here the vegetation

is of the true salt-loving type. The two dominants, *Atriplex lentiformis* and *Atriplex polycarpa,* are not evenly intermixed but form pure stands, often 50 feet in diameter. *Dondia sufferescens,* the salt blite, is also common and tends to form pure communities. Here and there are scattered the mesquites *(Prosopis glandulosa),* approximately one for each 50 feet. Around the Indian adobe houses one finds occasional clumps of *Populus fremontii.*

In contrast to most Atriplexes, *Atriplex lentiformis* (Fig. 6) forms a very luxuriant growth of almost impenetrable compactness. Fig. 7 shows a typical stand of *Atriplex polycarpa;* while it reaches only half the height of *Atriplex lentiformis* the stands are of equal density. The photograph of a pure growth of *Dondia sufferescens* (Fig. 8) was taken in the same area.

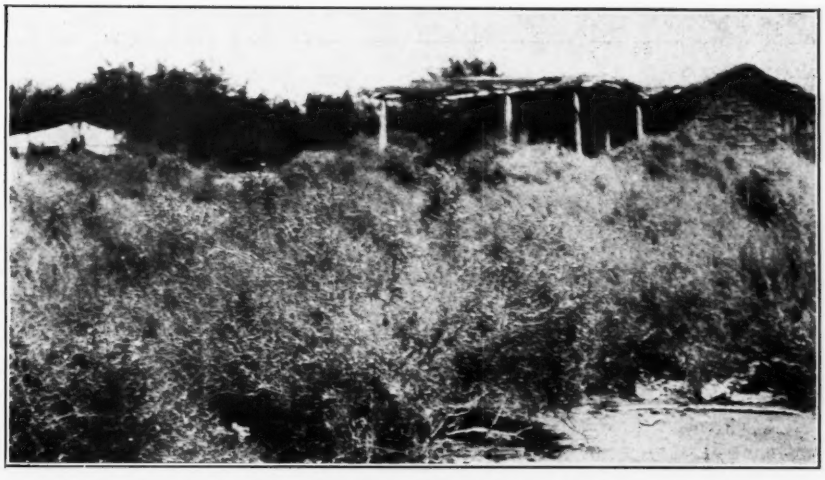

Fig. 7.—Pure community of *Atriplex polycarpa.*

SUMMARY AREA III

FAMILY		SPECIES		OCCURRENCE
SCIENTIFIC NAME	COMMON NAME	SCIENTIFIC NAME	COMMON NAME	
SALICACEAE	Willow Family	*Salix nigra*	black willow	occasional
CHENOPODIACEAE	Saltbush Family	*Atriplex lentiformis*	lenscale	abundant
		Atriplex polycarpa	cattle spinach	abundant
		Dondia sufferescens	salt blite	very common
LEGUMINOSAE	Pea Family	*Prosopis juliflora var. glandulosa*	honey mesquite	frequent
		Prosopis juliflora var. pubescens	screw bean mesquite	frequent

AREA IV is located about one mile southeast of town in a slight wash. Here is found the common arid vegetation of this altitude with the creosote bush *(Larrea tridentata var. glutinosa)* and cattle spinach *(Atriplex polycarpa)* occurring as abundant codominants. This is the

only area in which *Franseria dumosa* is found, and here it is very rare. A rather common grass, appearing for the first time, is *Hilaria rigida*. It can be found for six or seven miles southeast.

SUMMARY AREA IV

FAMILY		SPECIES		OCCURRENCE
SCIENTIFIC NAME	COMMON NAME	SCIENTIFIC NAME	COMMON NAME	
GRAMINEAE	Grass Family	*Hilaria rigida*	galleta	common
CHENOPODIACEAE	Saltbush Family	*Atriplex polycarpa*	cattle spinach	rather abundant
LEGUMINOSAE	Pea Family	*Acacia greggii*	catclaw	common
EUPHORBIACEAE	Spurge Family	*Euphorbia (species)*		rare
COMPOSITAE	Sunflower Family	*Franseria dumosa*	burro weed	rare
		Hymenoclea salsola		few
		Other compositae		scarce

Fig. 8.—Typical growth of *Dondia sufferescens*.

AREA V. In order to determine the pollen factor from the southeast an area three miles from town was studied. Here, as in Area IV, *Atriplex polycarpa* is the dominant and *Larrea tridentata* is very common. A few species of *Opuntia* begin to come in at this altitude.

AREA VI. In this section is included the entire central portion of the town, the only area containing cultivated plants. Nearly all of the homes have lawns of *Cynodon dactylon*. There are many shade trees along the streets and in the park at the railroad station.

In this area the most important species are the following:

Grasses: *Cynodon dactylon*, Bermuda grass, rather abundant.

Ornamental Shrubs: *Oleander (species), Kochia scoparia,* firebush or summer cypress, few, other shrubs, rare.

Trees: *Populus fremontii,* Fremont cottonwood, abundant. *Phoenix dactylifera,* date palm, occasional. *Washingtonia filifera,* California fan palm, rare. *Schinus molle,* pepper tree, frequent. *Parkensonia microphylla,* male palo verde, occasional. *Prosopis juliflora var. glandulosa,* honey mesquite, frequent; *P. var. pubescens,* screw bean mesquite, few. *Melia azedarch,* umbrella tree, very scarce.

AREA VII. Just west of town there is a large cleared section along the highway, making it necessary to select an area two miles distant. Here again are found *Larrea tridentata* and *Atriplex polycarpa* as co-dominants. The latter continues to the river's edge, while on the north side of the river we again find the typical willow formation.

SUMMARY OF THE ENTIRE DISTRICT

In Needles and its vicinity the only species which are of importance in hay fever are included in the following list:*

GRAMINEAE, Grass Family.

+++ *Cynodon dactylon,* Bermuda grass. + *Hilaria rigida,* galleta.

SALICACEAE, Willow Family.

++ *Salix nigra,* black willow. ++ *Populus fremontii,* Fremont cottonwood.

CHENOPODIACEAE, Saltbush Family.

++ *Atriplex elegans.* +++ *Atriplex lentiformis,* lenscale.

+++ *Atriplex polycarpa,* allscale, cattle spinach.

AMARANTHACEAE, Amaranth Family.

+ *Amaranthus palmeri,* Palmer's amaranth, careless weed.

LEGUMINOSAE, Pea Family.

Acacia greggii, catclaw.

Prosopis juliflora, var. glandulosa, honey mesquite, *var. pubescens,* screw bean mesquite.

COMPOSITAE, Sunflower Family.

+ *Franseria dumosa,* burro weed.

+ *Hymenoclea salsola.*

The hay fever problem of Needles may, therefore, be resolved into three potential hay fever seasons. Any cases of early spring hay fever would undoubtedly be caused by the pollination of *Populus fremontii* and *Salix nigra* which usually begin to pollinate in February. *Cynodon dactylon* and *Hilaria rigida* begin their pollination in March, thus making a potential late spring season. The real hay fever season

*Note.—+++ is most important; ++ important; + of minor or local importance.

is that which is due to the pollination of the Atriplexes. Of these *Atriplex lentiformis* and *Atriplex polycarpa* are extremely important, and *Atriplex elegans* is of minor importance. During this season there is also the *Acacia greggii, Prosopis juliflora vars., Hymenoclea salsola, Amaranthus palmeri* and *Franseria dumosa,* but these are of minor importance only.

The fact that the hay fever problem is a regional one is brought out vividly by the comparison of Needles with the nearest town of any size, that of Kingman, Arizona, about 60 miles east and at an elevation of 3,328 feet. Here *Franseria tenuifolia* is very common while it did not occur in Needles. The same is true of *Salsola kali,* Russian thistle, which is very abundant in Kingman. On the other hand, *Atriplex lentiformis,* probably the most important hay fever plant in Needles, was not found in Kingman.

In comparing Needles with Barstow, a town 160 miles west, with an altitude of 2,424 feet, the differences were just as striking. For example, Russian thistle, *Salsola kali,* and salt grass, *Distichlis spicata,* were found in abundance. The ragweeds, of no consequence in Needles, were very common. Moreover, *Atriplex canescens,* given by many biologic supply houses as the important *Atriplex* in the southwest, was entirely lacking from the Needles vegetation and apparently is unimportant in Kingman and Barstow.

CONCLUSIONS

This survey applies to an isolated desert community. Its proximity to a river considerably modifies the usual desert flora. The rainfall and climatic conditions militate against any sharply defined seasons of pollination. In general the cottonwoods and willows are most significant during the early months of the year. Bermuda grass, usually absent from the typical desert vegetation, grows abundantly in the meadow adjacent to the river and undoubtedly will reach during the spring a significant level of pollination and maintain this throughout most of the remainder of the year. In that portion of the area which is typically desert the physiognomy is made up of Atriplexes in practically pure stands.

It has been pointed out that this flora is distinct for the community under study and is not at all like that of the locality mentioned to the east and to the west. The factors we have emphasized as being significant in hay fever are certainly not included in the list usually published by the several biologic supply houses. This further emphasizes the need for a detailed survey of each area and the impracticability of including this or any other community under the broad term, "Pacific Southwest."

Hay fever and similar conditions among individuals in this area may be due to trees, Bermuda grass, and to two members of the genus

Atriplex. In contrast to the central west and the rocky mountain areas where ragweeds and sagebrush respectively are important etiologic agents, Needles has a true *Atriplex* hay fever problem. The sensitivities of individuals exposed to an atmosphere contaminated with this and other chenopod pollen have been investigated and will form the basis of another report.

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ENTERAL ABSORPTION OF THE ANTIGEN AND THE APPARENT FAILURE OF ANTIGEN SECRETION IN HUMAN MILK*

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THE eczema that occurs in the breast-fed infant presents one of the most baffling problems which the physician encounters. The secretion of certain drugs by the breast and the earlier belief that immune bodies were passed through colostrum, have led to the supposition that (allergic) antigens might likewise be secreted in the breast milk. Clinically, this appears substantiated by numerous reports. Experimentally, Shannon[1] claimed to have obtained evidence of egg white in breast milk, since the latter on injection of guinea pigs sensitized to egg white, produced an anaphylactic response. Stuart,[2] however, in a more exhaustive study, was unable to confirm Shannon's work.

That the antigens may be absorbed unaltered from the intestinal tract has been demonstrated by Schloss and Worthen,[3] who followed precipitin response after oral ingestion. There is, however, some discrepancy between precipitin (anaphylactic antibody) and the substance responsible for the skin test of allergy (reagin). There is also the difficulty in drawing conclusions referable to human allergy from experimental animal anaphylaxis.

Walzer,[4] Gay and Chant,[5] and others have, however, demonstrated the enteral absorption of allergic antigen by a simple modification of the Prausnitz-Küstner technic. Since this offers a closer parallel with human allergic phenomena, the following experiments were devised to test by this method the secretion of antigens in the breast milk.

REPORT

Thirty-six patients in the St. Louis Maternity Hospital were kept on an egg-free diet for two days and on the second day 0.1 c.c. of egg-sensitive serum was injected intracutaneously into the anterior surface of the forearm of the mother and of her newborn infant. The mother was not given egg until the fourth day, when she was allowed an egg-rich diet, and the arms of the mothers and babies were watched at intervals of fifteen minutes during that day and evening. In all of the cases studied the mothers reacted by the production of marked

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pruritus within forty-five minutes to an hour at the site of the injection, followed by marked erythema and wheal formation after the ingestion of egg. None of the infants showed a reaction at the site of the injection. Any type of reaction, such as erythema, wheal or pseudopod, was watched for. In order to prove that the reagins were present at the sensitized area, the babies were fed 2 ounces of albumin water and within twenty to thirty minutes after the feedings there appeared a marked reaction consisting of an erythema and wheal formation.

In another series of cases (11) the mothers and their infants were injected as above with the egg-sensitive serum and the mothers were kept on an egg-free diet for two days, and an egg-rich diet for two days. No reactions occurred on the infants' arms while the same type of reaction that was observed in the first series was noted on the mothers soon after the ingestion of the egg. In this group, also, the babies were fed albumin water to show that the reagins were present at the sensitized area and an erythema and wheal formation occurred in all just as in the previous series.

In order to get a greater concentration of the antigens in the mother's milk we gave an egg-rich diet to two mothers for three days without injecting the egg-sensitive serum into their arms. At the time these mothers were getting the copius supply of egg in their diet, four other mothers and their infants were injected with the serum, the latter mothers being kept on an egg-free diet. On the fourth day the milk was pumped from the breasts of the mothers who had been receiving the egg-rich diet and given to infants of the mothers who had received no egg. No reaction occurred on the infants' arms until after the feeding of the albumin water.

CONCLUSION

From these experiments it will be seen that breast milk fails to transmit sufficient antigen for demonstration of passive transfer to the average newborn infant, though direct feeding of the antigen produces a striking reaction.

NOTE

Since the completion of this study, Donnally[6] has reported experiments with conclusions quite contrary to those reported above. Collecting the breast milk from nursing mothers fed egg-rich and egg-free diets, he used refined portions of these respective milks as antigen and control for the Prausnitz-Küstner technic. The milk collected during an egg-rich diet gave reactions greater (in most instances) than that collected on the egg-free diet.

While we are planning to repeat Donnally's experiments, certain criticisms seem warranted. The fact that the "control" gave reac-

tions suggests that despite the efforts at purification, the milk contained substances which themselves were capable of inducing reactions, perhaps of a nonspecific type. If such were the case, a variability of milk may be possible without attributing any differences to the presence of egg albumen. Differences in reactions should have had the additional control of passive transfer at a site injected with a nonsensitive serum. The manipulation of the milk before injection introduces objectionable factors, since we know that chemical irritants and physical changes may cause reactions. While there may be a difference in titer in Donnally's serum and that used by us, we believe that Walzer's technic could have been applied and that the feeding of the breast milk to recipients would have eliminated part of the objectionable technic. The response could then be measured against that from varying strengths of albumin water given by mouth.

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REPORT OF 100 CASES OF LOCAL PASSIVE TRANSFER OF HYPERSENSITIVENESS*

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HYPERSENSITIVENESS conveys the opposite meaning of immunity, although the underlying mechanism is identical in both conditions; namely, an antigen-antibody reaction. While it is generally admitted at the present time that hypersensitiveness is an immunologic disease, it has not as yet been fully accepted that the antigen-antibody reaction is the underlying basis of the various allergic manifestations.

In the course of the last two and a half years, I employed the method of local passive transfer in a series of 100 cases, and before reporting my own observations I wish to review some of the literature on the subject of local passive transfer.

The study of local passive transfer in the human is an application of the principle of antigen-antibody reaction derived from the study of anaphylaxis in animals. In order to have a clearer understanding of local passive transfer, I find it necessary to refer to the study of anaphylaxis in animals.

The term anaphylaxis was originated by Richet[1] in 1902 as an antithesis to prophylaxis. From a series of experiments performed together with Portier and Hericourt, Richet recognized a distinct dependence of the hypersusceptible condition upon a preceding inoculation with the same substance and that a definite incubation time must elapse after the first injection before susceptibility is developed; thus, they defined the most important criteria of anaphylaxis.

However, a clear statement of the fundamental phenomena of anaphylaxis was given by Flexner[2] in 1894 as follows: "Animals that had withstood one dose of dog serum would succumb to a second dose given after a lapse of some days or weeks, even when this dose was sublethal for a control animal." This is a perfect example of active sensitization.

Later it was shown that if the blood of the actively sensitized animal is transferred to a normal animal before the second lethal dose is given, and when an initial dose of the same protein is then given to the normal animal, it will develop symptoms of shock as the actively sensitized animal does; thus clearly showing that something preformed was transferred from the blood of the sensitized animal; namely, antibodies specific for the protein used. This clearly demonstrates passive transfer in animals.

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*From the Michael Reese, Mt. Sinai and University of Illinois Research Dispensaries.

Read before the Chicago Society of Allergy on February 16, 1931.

Otto[3] in Germany and Rosenau and Anderson[4] of the United States Hygienic Laboratory took up this problem independently and arrived at the same conclusion.

Arthus[5] in 1903 demonstrated local hypersensitiveness due to the repeated injections of horse serum in rabbits, now known as "Arthus phenomenon."

Von Pirquet[6] in 1906 introduced the term "allergy" to designate the altered reactivity in human or animal which takes place through recovery from disease or through treatment with foreign substances.

However, Prausnitz and Kustner,[7] 1921, were the first to apply the facts of anaphylaxis to human allergy by transferring hypersensitiveness locally. They injected the serum of one patient sensitive to egg and another patient sensitive to fish, into the skin of normal individuals and found that the areas so prepared would react with an immediate urticarial reaction when the corresponding protein extracts were applied to them. This constituted the first instance of local passive transfer of hypersensitiveness and opened a great field for exploration of allergy, since it clearly demonstrated the phenomenon of an allergic reaction to be due, fundamentally, to antigen-antibody reaction. De Besche in 1923 demonstrated antibodies in serum disease by means of local passive transfer. Later Coca[8] and his associates have greatly elaborated this work and named this antibody "reagin" claiming it to be peculiar only to human hypersensitiveness and distinct from other antibodies.

The technic usually employed is as follows: Blood is drawn from the allergic individual in the usual manner, defibrinated, centrifuged and the serum drawn off. About 0.1 c.c. of the serum is injected intradermally into the surface of the arm or forearm of a normal individual. Usually, after twenty-four hours the antigen is applied directly to the sensitized area by the scratch or intradermal method or, in the case of foods, indirectly through the gastrointestinal route; a method developed by Walzer.[9] The other arm is used as a control. Positive reactions, characterized by urticarial wheals, occur within five to twenty minutes after application of antigen by the direct method. Delayed reactions are met with occasionally.

Concerning the antibody (reagin) in human hypersensitiveness, we may state that primarily it is formed by, and usually adherent to, a certain group of cells known as "shock tissue." When, however, the cellular concentration has reached a certain point, the excess becomes free in the blood (circulating antibodies) and still keeps its power of specific reactivity with its particular antigen as is seen when transferred to the skin of normal individuals. Reagins are comparable to ferments in that they have no definite structure as far as is known, and can be regarded as new functions of the cells as a result of antigenic stimulation.

Some of the physical properties of these antibodies are as follows: they are thermo-stabile; heating of the reagin-containing serum to 56 to 60 degrees Centigrade for one-half hour causes but a slight loss of its transferring power. Reagin-containing serum will keep in the ice box for many months, and I have tested a reagin-containing serum one year old that still reacts considerably to its antigen (cotton seed). The incubation period of these antibodies is very short, due to their great affinity for the cells of normal skin. They rapidly become anchored and fixed at the site of the injection, and one may obtain a considerable reaction within twenty to thirty minutes. They may remain at the passively sensitized site up to sixty days. When the concentration of the antibodies is great, as during an attack, it may require several injections of antigen (of a moderate strength) to neutralize the sensitized area (quantitative). Such neutralization of antigen and antibody in vivo is highly specific, and is a very useful differential procedure in cases of multiple sensitiveness. After complete desensitization to one antigen the same area will react with a second antigen with undiminished intensity. This fact is utilized in testing a great many proteins on a relatively few sensitized sites.

Neutralization of antibody by antigen in vitro can be accomplished provided undiluted reagin-containing serum obtained from the patient during an attack is used and when the antigen is not too concentrated. There is no visible precipitation in the test tube during neutralization of antigen and antibody, immediately or after twenty-four hours of incubation or room temperature. Slight heating and agitation have no effect. A serum so neutralized may no longer passively sensitize.

Similarly, the antigen so neutralized in vitro by the corresponding antibody may no longer produce a local reaction either on the skin of the sensitive individual or on the normal. Excluding the quantitative factor as one of the possible causes, there still remains the possibility of an additional factor, namely, the maximum effect of the antibody may depend upon the presence of a complement.

Although some allergists speak of a definite parallelism existing between antibody (reagin) content of the blood and skin sensitivity, I am inclined to believe that the opposite is the rule in cases where the equilibrium is upset. For instance, during an attack of asthma the skin oftentimes becomes refractory and at the same time the circulating antibodies increase. This is the most significant fact, and I would like to stress it as a cardinal point in cases of attempted passive transfer. It may be the only time during which the antibodies are present in circulation. This fact partly explains why the skin becomes refractory during an attack because the antibody is neutralized by the antigen, bringing on a state of exhaustion of the shock tissue. Another fact to be remembered in this connection is

that in using the skin of normal individuals we often encounter a refractory type of skin. Such skins are a counterpart of the other extreme, namely the hyperirritable. In both instances a passive transfer may fail.

A detailed analysis of the results with passive transfer is as follows:

TABLE I

CLINICAL MANIFESTATION	POSITIVE RESPONSE	NEGATIVE RESPONSE	TOTAL CASES
Asthma	41	13	54
Hay fever	22		22
Urticaria		10	10
Vasomotor rhinitis	2	6	8
Angioneurotic edema		3	3
Migraine		2	2
	65	34	99

Table I shows the distribution of the cases with respect to the clinical manifestations. The percentage of positive diagnoses is about 65 per cent. The diagnosis was usually substantiated in each case by history and skin test. However, in 6 cases of asthma and 2 cases of hay fever the skin tests were totally negative. In 3 cases of asthma I was able to make a bedside diagnosis, that is within twenty-four hours, while the patient was having paroxysm. In 2 cases, in addition, the skin was affected by severe eczematous eruptions, where no skin tests were possible for three weeks after. Of the 13 cases of asthma that were negative on passive transfer some did show skin reactions that were neither marked nor consistent with the history and were considered bacterial. Their ages ranged from forty to forty-five years and up, while in the cases of successful passive transfer the age incidence was not over forty to forty-five years. The youngest case of successful passive transfer was that of a child sixteen months old, sensitive to egg. In hay fever, the result of transfer is 100 per cent positive and age plays no part. In one instance the patient was sixty-five years old, having had hay fever for two years only. Passive transfer done during the hay fever season showed skin reactions of much greater intensity. Of 8 cases of vasomotor rhinitis one was due to duck feathers and another to orris root. The latter, however, had in addition hay fever of the fall type. None of the cases of urticaria, angioneurotic edema, and migraine were positive.

Table II shows the distribution of the cases as to their etiologic factors, degree of reaction, and the associated clinical manifestations. The most striking finding in the series is the preponderance of positive reactions in the cases of inhalants and the relatively few in cases of foods and bacteria. This fact perhaps can be explained on a biologic basis, namely, the more heterogenous the character of the etiologic substance, the more readily is demonstrable antibody produced.

Similarly, the degree of skin reactions on passive transfer in the inhalant group were more intense. In the majority of cases these were accompanied by pseudopods, and practically in every instance they exceeded the skin reaction on the allergic individual. However, in the case of foods and bacteria the reactions were of a mild degree characterized by erythema, and in no instance were pseudopods observed.

I would like to mention a fact regarding desensitization as studied by skin test and passive transfer in about 8 to 10 cases, watched over a period of two years in some instances. The clinical symptoms are the first to disappear and the skin sensitivity is the last. On the whole, the circulating antibody runs almost parallel to the skin sensitivity, excepting during attacks, but in a few instances it disappears somewhat before the skin sensitivity; although the latter may not disappear entirely, but greatly diminish.

TABLE II

CLINICAL MANIFESTATION	CAUSATIVE SUBSTANCE	NO. OF CASES	ASSOCIATED MANIFESTATION	DEGREE OF REACTION
Asthma	Feathers	7		From +++ to ++++
	Orris root	3		++++ very marked
		2	Hay fever	++++ very marked
		1	Eczema	++++ very marked
		1	V-M-rhinitis*	++++ very marked
	Cotton seed	3		++++ very marked
		1	Eczema	++++ very marked
	Silk	1		+++ to ++++
		1	Hay fever	+++ to ++++
		1	Eczema	+++ to ++++
		1	V-M-rhinitis	++ to +++
	Dog hair	3		++++ very marked
	Cat hair	1	Hay fever	++++ very marked
		1	Eczema	++++ very marked
	Pyrethrum	1		++++ very marked
		1	Eczema	+++
	Wheat	1	Hay fever	++ to +++
		1	Eczema	++
	Egg	1		++
		1	Eczema	++
	Fish	2		++ to +++
	Horse dander	1		+++
	Tobacco	1		++
	Boxwood	1		++++ very marked
	Sawdust	1	Hay fever	++ to +++
	Mattress extract	1		++++ very marked
	Bacteria (staph. aur.)	1	Rheumatism (old chronic)	++
Hay fever	Ragweed Pollen	14		+++ to ++++
	Ragweed pollen	6	Asthma	+++ to ++++
	Timothy Pollen	1		+++ to ++++
	Orchard gr. Pollen	1		++
V-M-rhinitis	Feathers	1		++ to +++
	Orris root	1	Hay fever	+++
		65		

* = Vasomotor rhinitis.

The number of proteins applied to different cases varied; in some instances as many as 50 proteins were used. The methods included both the scratch and intradermal, depending on indications in individual cases. The serums of many patients were tested on several occasions, as for instance before, during, and after attacks. The recipients employed were normal individuals, having no history of allergy, and as a rule, no relatives (immediate) were used. In many instances one serum was transferred to several normal individuals, in some cases as many as 5; but usually I considered this as one case of passive transfer.

CONCLUSION

My chief purpose in presenting this paper is to stimulate a greater interest in passive transfer in order to include it in the recognized diagnostic procedures in cases of allergy. I do not know of any contraindication except probably the technical work connected with its employment, especially in infants. On the other hand, I should like to point out some of the distinct advantages. In employing the skin as an index of sensitivity we must remember that the skin is an organ which may not take part in the general sensitiveness of the individual or it may be the only organ involved. When in addition we consider the number of totally refractive and hyperirritable skins, we can readily appreciate that the percentage of cases in adults where the skin tests are reliable is rather limited in number. While I do employ all known procedures in diagnosis, such as history-taking and skin tests before doing a passive transfer, I feel at the same time that in a great many cases such criteria are totally inadequate and at times even misleading. At best, history may give a clue, which when substantiated by positive skin findings leads one to a presumptive diagnosis.

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Society Proceedings

CHICAGO SOCIETY OF ALLERGY

The regular monthly meeting of the Chicago Society of Allergy was held April 20, 1931.

Program

A New Method of Nonspecific Treatment of Allergic Disease. Preliminary Report. S. M. Feinberg, M.D., S. L. Osborne, M.D., and M. L. Afremow, M.D.

Based on the clinical observation that fevers of infectious origin frequently check temporarily the symptoms of allergic disease, especially asthma and hay fever, the authors were led to believe that fevers artificially produced might be serviceable in some cases of allergy. The methods in vogue for the production of artificial fever, such as intravenous protein injections, etc., were considered too dangerous and not sufficiently controllable. The production of hyperpyrexia by diathermy with special electrodes, as is used in the treatment of general paresis, induced the authors to believe that the same method might be of value in allergic cases.

In treating asthma patients, maximum temperatures of 103° F. to 105° F. were reached, with a sustained temperature of over 101° F. for a period of four to eight hours. Although only a few cases of asthma have been tried thus far, the results are encouraging. In some instances, the symptoms were completely relieved, in others there was amelioration; the duration of relief or improvement is variable. In some instances, the patient reacted rather strenuously to the treatment, but so far, no apparent harm has been noted. Usually, twelve to twenty-four hours after treatment, the patient recovered from all discomfort associated with the fever. The authors stress the fact that there will have to be a very careful selection of cases for this type of treatment although the criteria by which such selection is to be made has not been definitely determined. This experimental work is also being carried out in hay fever and other allergic conditions.

A Study of the Reactions in Nonsensitive Skin of Mixtures in Vitro of Reagin and Atopen. Francis L. Foran, M.D., and Meyer R. Lichtenstein, M.D.*

The authors present a method for the measurement of the square surfaces of wheal and erythema areas. Comparison between the re-

*From the Allergy Clinic of Rush Medical College.

actions of homologous and nonhomologous mixtures can then be expressed as a simple ratio of the square surfaces of the reacting areas. Every homologous mixture is doubly controlled by a mixture of the serum with nonhomologous atopen and a mixture of the atopen with nonhomologous serum. The mean ratio of specific to control reactions is thus established for 94 readings at fifteen minutes, of approximately 1.0; for 87 readings at sixty minutes, of approximately 3.0; and for 56 readings at ninety minutes, of approximately 6.0.

In contrast to similar studies, this procedure furnishes a simple objective comparison of reactions; a relative exclusion of factors of variation, such as differences in skin reactivity, by averaging a large number of comparisons in one mean ratio; and a consideration of an important time factor. The authors conclude that mixtures in vitro of reagin and atopen do react when injected into nonsensitive skin; that neutralization does not occur in the test tube; that the mixtures are probably inert in the test tube and react only after injection; and that such a reaction does not essentially differ from the Prausnitz-Küstner phenomenon.

Department of Reviews and Abstracts

Selected Abstracts

Food Allergens. Vaughan, W. T.: Jour. Immunol. **20**: 313, 1931.

Sensitization tests are discussed in considerable detail. Attention is then turned to those cases where the suspected allergenic food cannot be identified by skin test. In such instances it seems apparent that elimination diets should be tried. Various diet lists have been proposed by different authors based on the principles of the use of the less usual foods and foods to which people usually are found to be nonsensitive. Foods to which an individual has been found sensitive by skin test are, of course, omitted. At the same time, the diets must be adequate as maintenance diets. In the opinion of the author the procedure for the selection of trial diets must be radically altered and should be based more upon a genetic classification of foods in which foodstuffs presumably derived from a common ancestor, or closely related ancestors, are grouped together.

By experience, it was found:

(a) If one is sensitive by test to one member of a food group and this member is found on trial to be allergenic, other members of the same group may produce symptoms, even though their skin reactions are negative.

(b) One may give a positive reaction to one member of a group which, on trial, is found to produce no symptoms, while other members of the same group, reacting negatively, do produce symptoms when eaten.

(c) One may manifest negative skin reactions to all the individual members of a food group but give a positive reaction to the group mixture. In this case, certain individual members, even though reacting negatively, may be responsible for symptoms.

In illustration of the trial diet based on genetic classification, the case is given of a patient sensitive to green peas. If he is thus sensitive, it is maintained that he should watch or avoid the various beans, lentil and peanut. To recommend lentil simply because it is a less usual food would be a faulty procedure. Various other illustrations are given.

The Hypochlorhydria of Asthma in Childhood. Bray, G. W.: Quarter. Jour. Med. **24**: 181, 1931.

It is pointed out that from the earliest times "digestive upsets" have been noted by all observers in association with asthma. Facts gleaned from clinical and experimental observation, which point to the undigested protein or its early cleavage products as responsible for allergic reactions, led the author to investigate the digestive functions in asthmatic children.

The fractional method of gastric analysis was used in over 200 cases of asthmatic children, varying in age from six months to twelve years. Normal children were used as controls. For several days prior to the test all medicines were stopped and no food was given the patient from the previous evening to the time of the test. Between 8 and 9 o'clock in the morning a stomach tube was passed and all the fasting juice drawn off, the tube remaining in position with the completion of the test. Two types of meals were used. (a) Oatmeal gruel (unsalted). The advantage of this meal is that it affords some estimate of the emptying time of the stomach and of the activity of the salivary ferments by means of the iodine test for starch. The disadvantages are that it is difficult to make the child swallow a pint of tasteless gruel, the preparation takes time, the quantity dilutes any juice secreted and so lowers the reading. (b) Alcohol. From 20 to 40 c.c. (depending upon the size of the child) of a 7 per cent dilution of ethyl-alcohol of neutral reaction in distilled water was passed by means of a syringe directly down the tube into the child's stomach.

The advantage of this meal is that it takes no time in preparation, is fed with no difficulty, and because of the small volume utilized does not introduce a dilution factor. Its one disadvantage is that no index is afforded of the emptying time of the stomach or of salivary ferment action.

Each fifteen minutes after the introduction of the meal, about 10 c.c. of gastric contents were drawn off through the tube until 12 specimens were obtained. A measured volume of each specimen in turn was titrated against a decinormal soda solution. The free hydrochloric acid was determined by titration to the end-point with dimethyl and the total acidity to the end-point with phenolphthalein. The results of 200 fractional gastric analyses in asthmatic children showed that in 9 per cent of the cases there was a complete absence of free hydrochloric acid over a period of two and three-fourths hours after the meal; in 48 per cent there was a pronounced hypochlorhydria and in 23 per cent a mild hypochlorhydria. Thus in 80 per cent of asthmatic children the response of acid gastric secretion was below the average normal. Closely similar results were obtained with both types of meals. Owing to its simplicity the alcohol meal is the one

advocated for routine use except in such cases as it is necessary to know the emptying time of the stomach.

It was noted that deficiency of acid secretion was more marked before the age of seven years, the curve tending to rise toward puberty. Comment is made upon the possibility of a relationship of this fact with the tendency to spontaneous cure which occurs during puberty, especially in boys. Sex did not appear to exert any pronounced influence on the frequency of hypochlorhydria. The usual causes of achlorhydria in young children are discussed. They include: (a) parenteral febrile diseases during the febrile stage and lasting into convalescence; (b) affections of the gastrointestinal tract. These causes were ruled out as nonoperative in the asthmatic children studied.

It was found, upon further investigation, that the incidence of hypochlorhydria is almost as frequent in inhalant cases as in food cases. The therapeutic indications are for acid treatment. Hydrochloric acid was given by mouth before or during meals, together with pepsin and a little syrup of senna. Commencing with a few minims of hydrochloric acid the dose was gradually increased until the optimum dose was from 20 to 30 minims three times a day. In achlorhydrics the dose even reached 60 to 90 minims. Results in several hundred cases of asthma showed:

(a) With acid therapy, plus the removal of the chief offending allergens as determined by skin tests, there is an immediate improvement in general health and freedom from attacks. If the acid therapy is continued for some months, the child remains free from attack and the medicine may be discontinued without further occurrence.

(b) With acid therapy alone, there is an immediate improvement in general health but slight attacks recur. After three or four months the attacks cease and while taking the medicine, the child appears well. But should the medicine be stopped or a slight infection supervene, attacks may, in some cases, recur. The author is applying acid therapy to all cases of allergy in which a hypochlorhydria is determined by gastric analysis.

The Chronic Effect of Epinephrin and Ephedrin on the Nasal Mucosa.
Fox, N.: Arch. Otolaryngol., **13**: 73, 1931.

Investigations were undertaken to determine whether in vasomotor rhinitis and chronic conditions of the sinuses the long-continued use of solutions of epinephrin and ephedrin had any deleterious effects. Observations were made upon the effect of these drugs on the nasal mucosa of rabbits after daily usage over a considerable period of time. Epinephrin chloride in solution 1:1000 and ephedrin hydrochloride in solution 1:50 were used for three months. Ten healthy, adult rabbits were used for each set of experiments and ten control animals were sprayed at the same time with a physiologic solution of

sodium chloride. Daily inspection was made of activity, nasal discharge, if any, and weight. Conclusions showed that little, if any, injury was caused by the daily spraying of the mucous membranes with ephedrin hydrochloride in dilution 1:50. Control animals sprayed with sodium chloride were uninjured. Considerable damage to the tissues, however, was caused by the daily spraying with epinephrin chloride in dilution 1:1000. Sections taken from the maxilloturbinate of animals thus sprayed showed considerable ante-mortem denudation. There was infiltration of the mucous membrane with some intraepithelial abscesses. These animals, after the third week of spraying, developed a mucopurulent discharge which remained to the end of the experiment. They were less active in their cages and lost weight.

Sodium Iodide in Hyperesthetic Rhinitis. Levy, A.: Arch. Otolaryngol. **13**: 97, 1931.

The author reports favorable results in cases of hyperesthetic rhinitis from the use of sodium iodide. A 3 per cent solution of sodium iodide is prepared, sterilized and allowed to stand several days in a white glass stoppered bottle until free iodine appears. Then 1 c.c. of the solution is injected hypodermically into the patient with sometimes a temporary exacerbation of the symptoms. Five days later the injection is repeated. If, after the solution has stood for some period of time, there is too much free iodide as shown by the increasing yellow coloration, the injection may become painful and the solution should be discarded and a fresh one prepared. If the result is favorable the injections should be repeated as necessary.

Fatal Anaphylaxis in Man. Sheppe, W. M.: Jour. Lab. & Clin. Med. **16**: 372, 1931.

A case of death following the administration of a foreign protein is described, with the findings at autopsy. The patient was admitted suffering from a bullet wound and received 1500 units of tetanus antitoxin subcutaneously. Approximately 20 minutes later he died, with marked dyspnea, before adrenalin could be administered. Autopsy showed the heart to be normal in size and shape; the stomach and liver normal; the spleen and kidneys normal. The lungs, however, were very large and voluminous and very light gray in color, with the surfaces much smoother than the lung surface usually seen at autopsy. Emphysematous areas were seen around the borders of both lungs. When the lungs were removed and put in a pan of water they floated high in the water and severance of bronchi did not lead to collapse of the lung.

It was subsequently ascertained that the patient was an ex-service man who had been wounded in France and presumably given tetanus antitoxin at that time. Fifteen other cases of death by what probably was some fatal anaphylaxis, previously reported in the literature, are analyzed.

Sensitivity in Treatment of the Eye. Biberstein, H.: Ztschr. f. Augenheilkunde, **71**: 283, 1930.

Experience has shown that in the treatment of the eye, certain substances that are used with some frequency, have been found on occasion to give rise to skin irritations. These are attributed to a sensitivity on the part of the patient to the substances or drugs used.

Quicksilver was found to give rise to a dermatitis. A case report is given. *Atropine*—A case report is given of a strong reaction—swelling of the face, particularly around the eyes and marked edema. The skin of the upper part of the body was reddened—following the instillation of atropine. A slighter reaction had been elicited by an atropine instillation twelve days previously. *Noviform* also produced reactions. *Cocaine* was found to be less frequently responsible. A case report is, however, appended. *Novocaine* seems seldom to offend. The author has never seen a reaction due to its use but notes the report by Jadassohn of two cases.

Such sensitivity as described can be a matter of heredity or it can be acquired. It can be specific for an individual substance or for a group of allied substances, or for several separate substances. It may also be nonspecific. The problem of sensitivity may be treated in three ways:

(1) The elimination of the allergen from the therapy and surroundings of the patient. (2) Substitution for the offending agent. Particular care must be taken to consider the possibility of a group specificity. Frequently the substitution may be effected by means of a change in the method application. (3) In the case of a material for which no substitution can be made and whose use is almost unavoidable, desensitization should be attempted.

Reactions of the Skin Following the Intradermal Injection of Arsphenamine. Moore, J. E., Woo, S. T., Robinson, H. M., and Gay, L. N.: Arch. Dermat. and Syphil. **23**: 74, 1931.

It is now generally believed that postarsphenamine dermatitis is a sensitization phenomenon. A brief résumé is given of work previously done on the subject. The present paper is an experimental investigation of intradermal testing for sensitization to arsphenamine. The tests were carried out with arsphenamine, neoarsphenamine and silver arsphenamine in dilutions of 1:1,600, 1:6,400 and 1:25,600 and

more generally with arsphenamine alkalinized in dilution 1:2,000. No marked differences in reactions were observed with varying concentrations of the drugs, so the results were grouped. About 0.06 to 0.08 c.c. was injected intradermally into the upper third of the flexor surface of the forearm. The reaction was observed for two hours and the patient frequently seen thereafter. Four groups of persons were used for test subjects:

a) Thirty-six normal controls.
b) Sixty-one patients with syphilis. Most of these had received therapeutic injections of arsphenamine without reactions of the dermatitic type.
c) Nineteen patients with allergic instability (hay fever).
d) Thirty-five patients who had suffered from postarsphenamine dermatitis.

Results showed a delayed reaction in about 60 per cent of normal persons. A similar reaction, less delayed and less severe, was observed in about 44 per cent of syphilitic patients under treatment. The diminished severity of the reaction and the shorter incubation period were attributed to the desensitizing effect of previous or simultaneous intravenous injection of arsphenamine.

Much more severe reactions of shorter incubation period were observed in all but one of the 19 patients with hay fever. This was interpreted not as sensitization to arsphenamine but as due probably to local autoinoculation of the sensitized person with his own antigen (pollen) in an inflamed area.

In the group of 35 patients with postarsphenamine dermatitis very strongly positive reactions appearing much earlier than in any of the other groups were observed in 70 per cent of those who had exfoliative type of dermatitis and in only 11 per cent of those who had other types of rashes.

In conclusion it is stated that a negative skin test in arsphenamine dermatitis does not necessarily indicate absence of sensitivity. It is possible that repeated tests might reveal such sensitivity but repeated testing is considered by the authors to be too dangerous to be justifiable, as alarming reactions have been elicited in this manner. Attempts at passive transfer of the sensitivity have so far been unsuccessful.

Diminution of the Vital Respiratory Capacity in Chronic Bronchitis, in Emphysema and in Asthma. Pescher, M. J.: Bull. de l'Acad. de Med. **104**: 53, 1930.

Spiroscopic methods for the measurement of vital capacity have shown that sufferers from bronchitis, emphysema, and asthma breathe insufficient air. It has furthermore been shown that such people have

an insufficient respiratory capacity even before the definite onset of this disease, predisposing them to the affection. This is not to say that other elements also do not enter into the complete picture of the syndrome.

It is suggested that the patient be trained to increase his breathing capacity. The patient breathes into the spiroscope, displacing the water to a certain graduation on the flask. This displacement shows three important things: (1) The patient's capacity whatever his malady; (2) what his vital capacity lacks in relation to the normal; (3) what is necessary, at the minimum, to recover normal capacity. Then the patient is taught better habits of breathing, and gradually increases his performance with the spiroscope until the displacement approaches nearer to the normal.

Apparent Specificity Among Streptococci and the Cause of Some Failures of Mixed Streptococcus Vaccines in the Treatment of Chest Colds and Asthma. Walker, I. C.: Jour. Lab. & Clin. Med. **16**: 539, 1931.

In previous papers it has been shown by the author that a mixed vaccine comprising the more prevalent varieties of streptococci for a given period had a considerable value as a curative and preventive in chest colds and asthma. Some cases, however, remained resistant to treatment. The cause of such failures is the subject of investigation of the present paper.

A group of papers is presented, wherein the patients had completed a course of vaccine consisting of a mixture of the 10 or 12 or more prevalent varieties of streptococci given as a preventive against chest and asthmatic colds. The treatment was unsatisfactory as the patients contracted a chest cold, or else had an attack of asthma with a cold, or the prevailing asthma was not benefited. Specimens of sputum were obtained and it was found that there were present one or more of the less prevalent varieties of streptococci or those in the 10 per cent or 15 per cent group which were not included in the general vaccine. Furthermore, the sputum contained none of the more prevalent varieties of streptococci or those in the 85 per cent or 90 per cent group comprising the preventive vaccine. One dose of autogenous vaccine (consisting of these less prevalent streptococci) brought prompt benefit or relief from symptoms. These cases would seem to argue for a specificity among streptococci.

Other cases are presented in which the sputum along with the less prevalent varieties, did contain one variety of the more prevalent streptococci used in the mixed vaccine. Failure in treatment with the mixed vaccine, it is pointed out, might have been due to the exclusion of the less prevalent types or to the insufficient quantity of the causative streptococcus. The strength or total bacterial count

and the dose of both the mixed and the autogenous vaccine were the same, but the quantity of each variety of streptococcus in each dose of the autogenous vaccine was five or more times greater than in the mixed vaccine due to the fact that the autogenous vaccine contained only one or two varieties of streptococci, whereas the mixed vaccine contained 10 or 12 varieties. Treatment with autogenous vaccine proved more satisfactory.

Pneumotachographic Studies—I. The Influence of Drugs on the Asthma Curve. Thiel, K., and Quednau, W.: Deutsch. Arch. f. klin. Med. **167:** 196, 1930.

Much work has recently been done upon the normal and pathologic pneumotachogram. Bretscheger outlined for the normal three different forms of pneumotachogram according to which the basic type of the normal individual may be ascertained. They are: (1) The coupling form; (2) the plateau form; (3) the peak form.

The pneumotachogram gives the following definite data on breathing: (1) The exact duration of inspiration and of expiration; (2) the maximum excursion and the exact point of its beginning; (3) the depth of breathing of the inspiration and the expiration; (4) the minute volume.

In recent years, the authors have studied by this means, the type of breathing of a considerable number of patients suffering from asthma and emphysema. Their observations as well as those of other workers show that the asthmatic curve differs from the normal most particularly in the great lengthening of the time of expiration. The asthmatic curve shows variations upon the administration of adrenalin and of atropin. Curves are given in illustration. An asthmatic, showing a typical curve, was given adrenalin. One minute after the dose, little change could be noted in the curve. Within fifteen minutes, however, a marked shortening of duration of expiration occurred. A contrary effect was obtained upon the curve by the administration of atropin. Comparative curves and charts are given.